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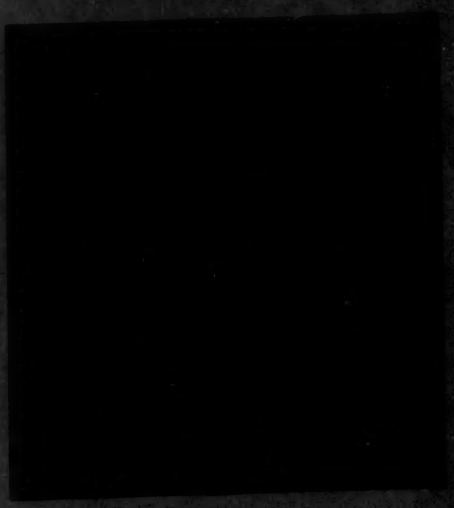

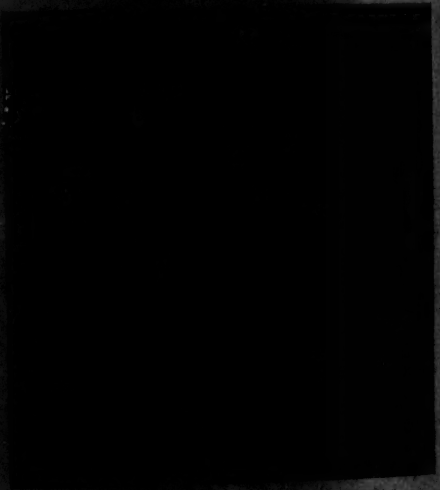

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COMMUNICATIONS

FURTHER CASES OF A FUNDUS DYSTROPHY WITH UNUSUAL FEATURES*

BY

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RECENTLY Sorsby and Mason (1949) described an unusual fundus dystrophy. The outstanding features were a bilateral central lesion of late onset and clearly genetic origin, with oedema, haemorrhages and exudates in the early stages, developing into generalized choroidal atrophy. The disease first came on in the early forties with a defect of central vision which intensified and spread to the periphery, though only in the most advanced cases did total blindness ensue. The genetic nature and dominant heredity of the lesion were shown by evidence of direct transmission over four generations.

The present report of a further family group, clearly belonging to the same clinical entity, serves to confirm and amplify the earlier description.

* Received for publication February 20, 1950.

Case Reports

Forty-four members of the family were examined and of these seven were found to be affected. Four more, now dead, were probably affected according to the evidence of several of their relatives. The significant findings concerning these affected individuals are summarized below and the available information about all those shown in the pedigree is given in the Appendix.

Living Members Found Affected

(1) *Mrs. Hy (III, 5 in pedigree), aged 68.*—Her left eye began to fail gradually between the ages of 40 and 45, the right followed between 45 and 50. Central vision failed rapidly. When examined her visual acuity was less than 6/60 in each eye, though her peripheral vision was good and she was able to move about freely. Her fundi are illustrated in Fig. 6 (*a*) and (*b*). The outstanding features are central scarring with masses of pigment, marked choroidal sclerosis spreading outwards from the centre, and a zone of relatively normal retina at the periphery. The disk is not atrophic, and the vessels, except where they supply the scarred central area, are not attenuated.

(2) *Mrs. Hd (III, 7 in pedigree), aged 63.*—Both eyes began to fail together at the age of 48. Central vision failed rapidly. When seen she was unable to read the largest type on the Jaeger reading chart, but her peripheral vision was good and she could get about her house easily. Her fundi, illustrated in Fig. 5 (*a*) and (*b*), were essentially the same as Mrs. Hy's.

(3) *Mrs. A. (III, 8 in pedigree), aged 57.*—Her left eye failed suddenly overnight, when she was 49; the right eye did the same at the age of 53. She says she was examined by an ophthalmic surgeon at that time, who found a macular haemorrhage in the right eye. Deterioration was rapid and when seen she had visual acuity of less than 3/60 in each eye and was registered blind. Nevertheless her peripheral vision was good and she could go about. The ophthalmoscopic appearances are illustrated in Fig. 4 (*a*) and (*b*). The lesion is rather less advanced than those of her sisters, and is seen to consist of three zones: a central scarred area, a zone of choroidal sclerosis spreading outwards, and a zone of relatively normal retina with some patterned exudates ahead of it.

(4) *Alfred B. (III, 10 in pedigree), aged 69.*—Both eyes began to fail at the age of 49 with black spots, photopsiae, and a central blur. Central vision failed quickly and he had to give up his work as a delivery-man within 4 years. When seen his visual acuity was less than 3/60 in each eye and he was registered blind, though his peripheral vision was good and he could move about freely. His fundi are shown in Fig. 7 (*a*) and (*b*). There is very extensive choroidal atrophy and sclerosis, but a narrow zone, less severely affected, persists at the periphery.

(5) *Edward B. (III, 13 in pedigree), aged 56.*—A central blur developed in both eyes together at the age of 51. When seen at the age of 56 his visual acuity was less than 3/60 in each eye and he was registered blind, but his peripheral vision was good enough to allow him to get about and do some work. His fundi (Fig. 3 (*a*) and (*b*)) showed a fairly early stage of the lesion with a considerable amount of normal peripheral retina and choroid.

(6) *Henry B. (III, 17 in pedigree), aged 48 (Proband).*—A shadow developed suddenly before both eyes at the age of 48, when he was first seen. He had to "look through it". Central vision was 6/9 part in the right eye and 6/12 in the left. Peripheral vision was unaffected. His fundi are illustrated in Fig. 1 (*a*) and (*b*). They represent the earliest stage observed in this family. The left eye shows only fine pigmentary mottling and white dots in the central area. In the right there is also some grayish oedema of the retina. No haemorrhages or massive exudates were seen. When he was re-examined after two years the fundi appeared unchanged and the visual acuity was the same. He complained, however, that the shadow was getting worse.

(7) *Harry Br (IV, 4 in pedigree), aged 52.*—A nephew of Mrs. Hy's and the only member of the younger generation affected so far. His right eye failed

suddenly with a central blur at the age of 49, and the left quickly followed it. Within three years he was unable to read even very large type, and this was his condition when seen. His peripheral vision was good and he could get about well. His fundi, illustrated in Fig. 2 (*a*) and (*b*), show the lesion still localized to the central area.

Deceased Members Reputed Affected

According to several of their children, George B. (II, 1), Frederick B. (II, 2), and Mrs. Br (III, I) were all "blind" before they died, from a central defect allowing them to get about easily, which came on between the ages of 40 and 50. *All three were parents of affected children and there can be no doubt they were affected themselves.*

According to her son, Mrs. L. (II, 4) died at about the age of 70, having been *blind for 25 years from a disease which came on suddenly in both eyes together.* It is probable that she was affected also.

Survey of Findings

Clinical Features.

Age of Onset.—In almost all the living affected members the trouble began between the ages of 45 and 55. The only exception was the left eye of Mrs. Hy which, she thinks, began to give trouble when she was between 40 and 45.

In the case of the deceased members reputed to have been affected the age of onset appears to have been between 40 and 50.

Mode of Onset.—In three cases this was described as sudden (Mrs. A. III, 8; Henry B. III, 17; and Harry Br IV, 4); in the others it was more gradual. The defect was central from the start, a central blur or "shadow", black spots or photopsiae being the usual complaint.

Course.—Failure of central vision was rapid in all cases and the four in which the times could be accurately established had central blindness within five years (Mrs. A. III, 8; Alfred B. III, 10; Edward B. III, 13; and Harry Br IV, 4). Peripheral vision, on the other hand, was not lost in any case. Even those certified blind were able to get about easily. No patient complained of night blindness.

Ophthalmoscopic Appearances.—The range of appearances in the living affected members is shown in the illustrations, which are arranged in order of age from the youngest, Fig. 1, to the oldest, Fig. 7.

The development of the lesion can be clearly seen. In the earliest stage observed (Fig. 1 (*a*) and (*b*)) the lesion involves the central area only with fine pigmentary mottling, white dots, and some oedema (Fig. 1 (*a*)). The macula becomes converted into a white scar with masses of pigment (Fig. 2 (*a*) and (*b*)) and the lesion spreads outwards with "unmasking" of the choroidal vessels and choroidal sclerosis preceded by fine patterned exudates (Fig. 4 (*a*) and (*b*)). The end stage is one of extensive choroidal

atrophy and sclerosis with massive pigment deposits, leaving always, in the cases here illustrated, a narrow peripheral zone of retina fit to function (Fig. 7 (*a*) and (*b*)). The disks do not become atrophic and the vessels remain of normal calibre except where they supply grossly atrophic retina.

Genetic Behaviour.

Direct Transmission.—This is shown over three generations. Affected individuals have been observed in two. Information as to whether either of the individuals in Generation I was affected is inconclusive. There is a family rumour of affected sibs on one side or the other in this generation who had affected descendants but it was not possible to trace them.

In no case was an affected individual known to have normal parents.

Proportion of Affected to Normal Sibs.—The significant data are summarized in the following Table.

TABLE

Individuals reaching the Age of 40, Offspring of Affected Parents

Generation	Unaffected			Affected		
	M.	F.	Total	M.	F.	Total
II	2	1	3	2	1	3
III	3	5	8	3	4	7
IV	2	6	8	1	–	1
Total	7	12	19	6	5	11

If the offspring of affected parents who have reached the age of 40 are taken, assuming that one of the parents in Generation I was affected, the proportion is 11:19, considerably lower than the 1:1 expected in a dominant affection. As has been seen, however, the age of onset in this family is nearer 50 than 40, so that genetically affected individuals in Generation IV may not have developed the lesion yet. If Generation II and III only are taken the proportion is 10:11, almost exactly the expected figure.

Sex Incidence.—Of the affected individuals, six were men and five women. Amongst the normal members of the family the proportion is 44:51.

FIG. 1(*a*).—Henry B. (III, 17), aged 48, right eye.

FIG. 1(*b*).—Henry B. (III, 17), aged 48, left eye.

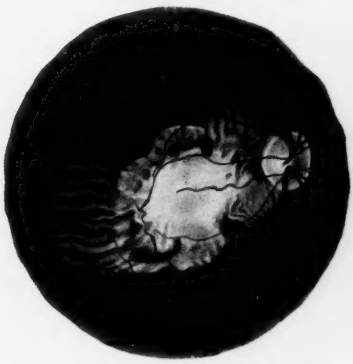

FIG. 2(*a*).—Harry Br (IV, 4), aged 52, right eye.

FIG. 2(*b*).—Harry Br (IV, 4), aged 52, left eye.

FIG. 3(*a*).—Edward B. (III, 13), aged 56, right eye.

FIG. 3(*b*).—Edward B. (III, 13), aged 56, left eye.

FIG. 4(*a*).—Mrs. A. (III, 8), aged 57, right eye.

FIG 4(*b*).—Mrs. A. (III, 8), aged 57, left eye.

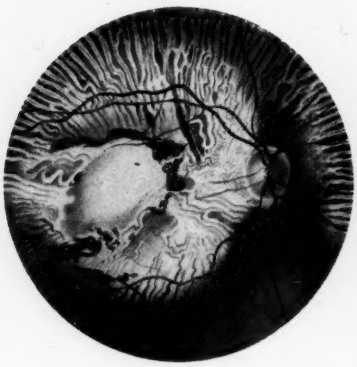

FIG. 5(*a*).—Mrs. Hd (III, 7), aged 63, right eye.

FIG. 5(*b*).—Mrs. Hd (III, 7), aged 63, left eye.

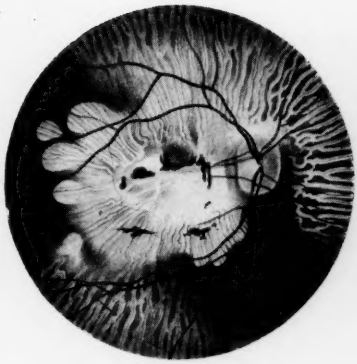

FIG. 6(*a*).—Mrs. Hy (III, 5), aged 68, right eye.

FIG. 6(*b*).—Mrs Hy (III, 5), aged 68, left eye.

FIG. 7(*a*).—Alfred B (III, 10), aged 69, right eye.

FIG. 7(*b*).—Alfred B. (III, 10) aged 69, left eye.

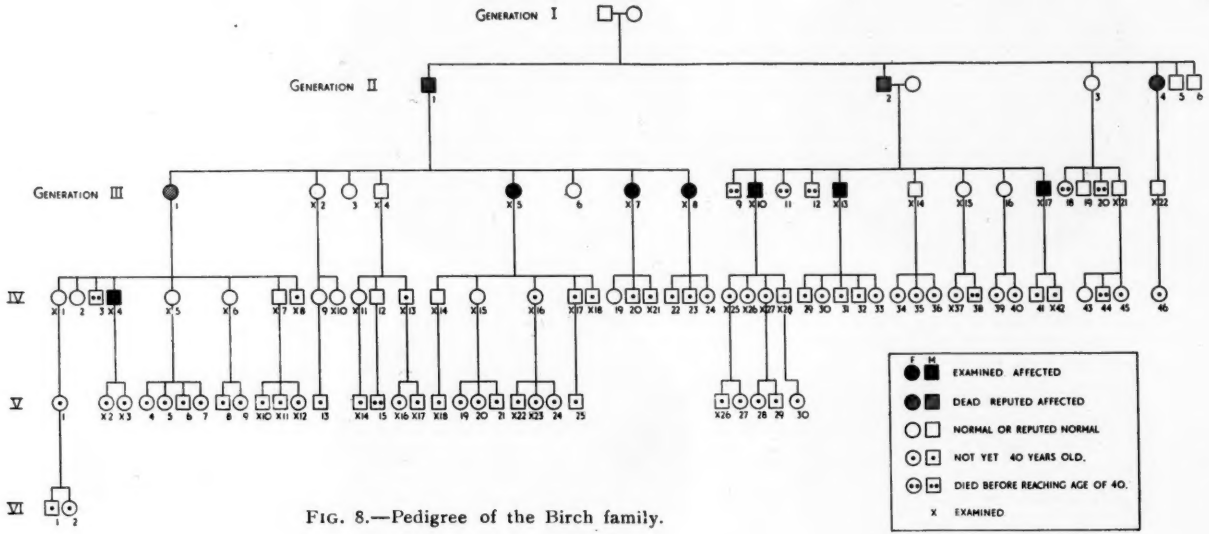

FIG. 8.—Pedigree of the Birch family.

Consanguinity.—None of the affected individuals is the offspring of a consanguineous marriage.

The genetic behaviour, in fact, corresponds well with that of an autosomal dominant gene.

The clinical and genetic characteristics in this family then, can be summarized as follows: *a central fundus lesion coming on in the late forties, of genetic origin and dominant transmission, progressing to central blindness but leaving peripheral vision free up to an advanced stage.*

Discussion

Comparison with the Cases of Sorsby and Mason.

No important differences exist. Certain minor variations may be mentioned.

Age of Onset.—In the earlier recorded cases this was more often in the late thirties or early forties than the late forties. The difference is not significant and only indicates that each family may have its own characteristic age of onset around which individuals vary.

Choroidal Sclerosis.—This feature is marked in all stages of the present family except the earliest (Henry B., Fig. 1). It is also an important feature of all the more advanced cases in the earlier report.

Haemorrhages and Exudates.—These were observed in the early stages of several of the previously recorded cases. No massive exudates were seen in this family but Fig. 1 (*b*) shows some oedema and Mrs. A. (III, 8) says she was examined in the early stages and found to have a macular haemorrhage. In a lesion running a subacute course, it is not surprising that the stages observed in one family do not exactly correspond with those seen in another. Over the whole range, and even excluding the history of macular haemorrhage given by Mrs. A., the ophthalmoscopic findings correspond closely to those in the earlier report.

Course and End Stage.—In both series loss of central vision within approximately five years was the rule, while peripheral vision was retained much longer, in the majority of cases up to the time of death. No member of the present family has yet become so blind as to be unable to get about. Four of Sorsby's cases, however, were reduced to total blindness or perception of light only. Two of these were complicated by glaucoma and the other two had had the disease for five to ten years longer than the longest affected member of the present family.

The course and end stage is, in fact, essentially the same in the two series of cases.

Proportion of Affected to Normal Sibs.—In Sorsby's families the proportion of affected to unaffected is higher than in the present family. Taking individuals over 40 years old the proportion of affected to unaffected was 60 : 45 as against 11 : 19 respectively. The difference is no greater than might be expected in so small a sample, and the combined figure (72 : 64) is quite compatible with the expected 1 : 1 ratio seen in simple dominant transmission.

Taking the picture as a whole, the resemblances between the groups of cases are so striking and the differences so insignificant that they are certainly examples of the same condition.

A Definite Clinical Entity.

The characteristics of this condition, of which there are now reports in six family groups, are so clear cut and so constant that it undoubtedly constitutes a definite clinical entity, which raises the following issues.

Frequency.—The frequency of the condition amongst the central fundus lesions of elderly people is difficult to assess. One case, the proband of this family, has been recognized during the last year at the Royal Eye Hospital.

Differential Diagnosis.—Sorsby and Mason have emphasized the fact that these lesions, although of abiotrophic nature, cannot be differentiated from inflammatory or metabolic disorders on ophthalmoscopic grounds. It can be seen from the illustrations that, depending on the stage at which the lesion is seen, a number of different diagnostic problems are raised. In the early stages, for example Fig 1 (*a*), the lesion may resemble the acute stage of a central choroiditis of toxic or infective origin; later it resembles the end result of such a choroiditis (Fig. 4). Disciform degeneration of the macula is suggested by Fig. 2 (*a*) and it is possible that Fig. 1 (*b*) might be dismissed as a senile lesion in a somewhat older man.

Prognosis.—Once the diagnosis is established the prognosis both for the patient and his children is clear cut. The progressive nature of the lesion emphasized by Sorsby is borne out in the series of illustrations given here. In the great majority of cases a severe central defect, often amounting to central blindness, developed within a few years. Since, however, the initial defect is central and spreads outwards, peripheral vision is the last to go. In most cases the patient remains able to get about until he dies. Of 39 observed cases in the two series only four were reduced to perception of light or total blindness, and two of these were complicated by glaucoma. The prognosis for the patient then is that he will lose central vision in both eyes within a few years but will probably always be able to get about.

If he has children there is an even chance that any given child will be affected later in life.

Possible Choroidal Origin.—Ophthalmoscopically the prominence of choroidal sclerosis in all but the early cases suggests that it may be the primary lesion and that the oedema, exudates, haemorrhages, and pigmentary disturbances seen in the early stages may be due to an underlying choroidal change. The orderly peripheral spread of the lesion, well illustrated in Fig. 4 (*a*) and (*b*) where a zone of choroidal sclerosis appears to be preceded by one of exudates, points in the same direction. The absence of night-blindness and the facts, already noted, that there is no optic atrophy and that the retinal vessels are not attenuated, support the view that the condition is probably not primarily retinal.

Theoretical Importance.—The theoretical importance of the recognition of this condition as a clinical entity lies in the fact that it is a disease of late onset with appearances usually ascribed to affections of environmental origin, and yet is clearly genetic. It is always difficult to establish the genetic origin of diseases coming on late in life because sibships are dispersed, sibs have died, and parents are dead. The recognition of one such disease in the mass of central fundus lesions of uncertain origin seen after middle-age points to the possible existence of others.

APPENDIX

Case Records (Pedigree Fig. 8)

Generation I.—Evidence concerning this generation is based on hearsay.

I, 1, reputed to have normal sight.

I, 2, reputed to have had some eye trouble but no details known. There was an unsubstantiated report that a sister of I, 2 named Bn., living at Flaunden, was affected and transmitted the affection to her children. An effort to trace this line was unsuccessful.

Generation II.

II, 1. George B., senior. Died aged 74 from a stroke. Reputed affected. He was blind but able to get about. A photograph of him as an elderly man in the possession of his daughter, Mrs. A. (III, 8), supports this idea.

II, 2. Frederick B., senior. Died aged 79. Reputed affected. He was blind before he was 50 and from "a similar condition".

II, 3. Mrs. Bt. Died aged 75. Not affected. She had some eye trouble, but was able to read and was not affected with the family disease.

II, 4. Mrs. Lt. Died aged about 70, probably affected. According to her son, she had been blind for 25 years before she died. Both eyes became affected suddenly.

II, 5 and 6. Two more sons of I, 1. According to their niece (III, 15), they had normal sight.

Generation III.

(1) *Children of George B., senior (II, 1, reputed affected).*

III, 1. Mrs. Br, of Chesham. Died aged 51 of stroke. Reputed affected. She was blind for three years before she died, with a central defect; she was unable to sew, but able to get about.

III, 2. Mrs. Bs, of Chesham. Aged 74. Was examined and found not to be affected. She is highly myopic, −15 and −20 D, but with glasses was able to read J4 with the right and J6 with the left eye. The fundus showed some myopic degeneration.

III, 3. Mrs. N. Died between the ages of 60 and 70. Reputed normal.

III, 4. Mr. George B., junior, of Chesham. Age 71. Was examined and found not to be affected. There is an old patch of juxtapapillary choroiditis in the right eye. The left eye was normal.

III, 5. Mrs. Hy, senior, of Chesham. Aged 68. Was examined and found to be affected. Her left eye was affected first between the ages of 40 and 45 and her right failed between 45 and 50. The onset was gradual. When seen, her central vision was quite gone but she was able to move about her house freely. See Fig. 6 (*a*) and (*b*).

III, 6. Mrs. Hs. Died at the age of about 65. Reputed normal.

III, 7. Mrs. Hd, of Chesham. Aged 63. Was examined and found to be affected. Started at the age of 48, both eyes more or less together. On examination her central vision was almost gone; she could not read Jaeger test types J18 but she moved about her house freely. See Fig. 5 (*a*) and (*b*).

III, 8. Mrs. A., of Chesham. Aged 57. Was examined and found to be affected. Her left eye failed suddenly overnight in June, 1940, when she was 49. She was seen by an ophthalmologist in November, 1940, who found haemorrhages at the macula. Her right eye failed suddenly, again overnight, in 1944 when she was 53. When examined she had central vision of less than 3/60 in each eye and was on the Blind Register. She had a good peripheral field and moved about easily but complained much of subjective disturbances such as photopsiae and black spots, more marked on slight exertion. See Fig. 4 (*a*) and (*b*).

(2) *Children of Frederick B., senior (II, 2, reputed affected).*

III, 9. William B., of Chesham. Died aged 32 of tuberculosis. Reputed normal.

III, 10. Alfred B., of Chesham. Aged 69. Examined and found to be affected. His trouble started at the age of 49 with black spots, flashes of light and central blur. He was obliged to give up his work as a delivery man at the age of 53. When seen his vision was less than 3/60 and he was registered blind. His peripheral field was good and the defect was central, for he saw better in a dim light and could get about easily. See Fig. 7 (*a*) and (*b*).

III, 11. Edith B. Died of tuberculosis, under 40. Reputed normal.

III, 12. Frederick B., junior. Died of tuberculosis, aged 38. Reputed normal.

III, 13. Edward B., of Uxbridge. Age 56. Was examined and found to be affected. His trouble first started at the age of 51. He is now registered blind but his peripheral vision allows him to get about and do some work. See Fig. 3 (*a*) and (*b*).

III, 14. Albert B. Aged 54. Seen by Dr. Joan Haythorne at the Royal Eye Hospital in December, 1948, and found to be normal with a visual acuity of 6/6 in each eye.

III, 15. Mrs. Florence D., of Harrow Weald. Aged 52. Was examined and found to be normal.

III, 16. Mrs. Hl, of Co. Durham. Aged 50. Reputed normal.

III, 17. Henry B., of Wandsworth. Aged 46 (Proband). Seen at the Royal Eye Hospital in September, 1947, when the trouble first started, complaining of a shadow in front of the eyes. Visual acuity unaided 6/9 part in the right eye and 6/12 in the left. Fundus pictures Fig. 1 (*a*) and (*b*) were made at this time. When seen again in December, 1949, visual acuity was unchanged and the fundus appeared the same. He complained, however, that the shadow was rather worse.

(3) *Children of Mrs. Bt (II, 3, reputed normal).*

III, 18. Female. Died before she reached the age of 40. Reputed normal.

III, 19. Male. Died aged 49 of heart disease. Reputed normal.

III, 20. Male. Died before he reached the age of 40. Reputed normal.

III, 21. Mr. Bt., of Chesham. Age 68. Was examined and found not to be

affected. His visual acuity was 6/12 in the right eye and 2/60 in the left. He had glaucomatous cupping of both discs; fundi were otherwise normal.

(4) *Child of Mrs. Lt (II, 4, reputed affected).*

III, 22. Mr. Lt, of Uxbridge. Aged 60. Was examined and found to be normal with a visual acuity of 6/6 in each eye unaided.

Generation IV.

(1) *Children of Mrs. Br (III, 1, affected).*

IV, 1. Mrs. U., of Amersham. Aged 59. Examined, normal.
IV, 2. Mrs. R., of Amersham. Died aged 56. Reputed normal.
IV, 3. Edward Br. Killed age 21. Reputed normal.
IV, 4. Harry Br, of Chesham. Aged 52. Examined, affected. His right eye failed suddenly in August, 1945, at the age of 49. The left became affected soon afterwards. He has been quite unable to read since April, 1946. On examination he had a severe central defect but good peripheral vision and was able to get about easily. See Fig. 2 (*a*) and (*b*).
IV, 5. Mrs. Rl, of Chesham. Aged 48. Examined, normal.
IV, 6. Mrs. M., of Chalfont St. Peter. Aged 45. Examined, not affected. Her fundus showed a fine generalized white mottling behind the retinal vessels in the equatorial and peripheral areas. The maculae were normal. Moderate myopia, reads J2.
IV, 7. George Br., of Chesham. Aged 42. Examined, normal.
IV, 8. William Br., of Chalfont St. Peter. Aged 36. Reputed normal.

(2) *Children of Mrs. Bs (III, 2, not affected).*

IV, 9. Mrs. Bl, of Chesham. Aged 53, reputed normal.
IV, 10. Mrs. W., of Chesham. Aged 51. Examined, not affected. Signs of old iritis in the left eye, otherwise normal.

(3) *Children of George B., junior (III, 4, normal).*

IV, 11. Mrs. Hy, junior, of Chesham. Aged 46. Examined, normal.
IV, 12. Leonard B., of Amersham Common. Aged 44. Reputed normal.
IV, 13. Sidney B., of Chesham. Aged 36. Examined, normal.

(4) *Children of Mrs. Hy, senior (III, 5, affected).*

IV, 14. Jack Hy, of Chesham. Examined, not affected. There were a few white spots in the macular area, probably within normal limits. Reads J1 with each eye.
IV, 15. Mrs. Ws, of Wendover. Aged 40. Examined, normal.
IV, 16. Mrs. Rd, of Chesham. Aged 39. Examined, normal.
IV, 17. Dennis Hy, of Chesham. Aged 26. Examined, normal.
IV, 18. Roy Hy, of Chesham. Aged 22. Examined, normal.

(5) *Children of Mrs. Hd (III, 7, affected).*

IV, 19. Mrs. Wn, of Maida Vale. Aged 40. Reputed normal.
IV, 20. Leon Hd, of Chesham. Aged 36. Reputed normal.
IV, 21. Terence Hd, of Chesham. Aged 30. Examined, not affected. Moderate myopia. Visual acuity 6/6 in each eye, with glasses. Normal fundi.

(6) *Children of Mrs. A. (III, 8, affected).*

IV, 22. Bertram A., of Chesham. Aged 32.
IV, 23. Raymond A., of Chesham. Aged 27. } Reputed normal.
IV, 24. Mrs. B., of Berkhamsted. Aged 45.

(7) *Children of Alfred B. (III, 10, affected).*

IV, 25. Mrs. He, of Chesham. Aged 37. Examined, normal.
IV, 26. Freda B., of Chesham. Aged 34. Examined, not affected. Moderate myopia, few vitreous opacities, normal fundi.

IV, 27. Mrs. Mr, of Chesham, Aged 32. Examined, normal.
IV, 28. Cecil B., of Chesham. Aged 26. Examined, normal.

(8) *Children of Edward B. (III, 13, affected).*

IV, 29. Frederick B., tertius, of Hillingdon. Aged 28.
IV, 30. Phyllis S., of Kingsbury. Aged 25.
IV, 31. Dennis B., of Chesham. Aged 23.
IV, 32. Peter B. Aged 16.
IV, 33. Pauline B. Aged 15.
} Reputed normal.

(9) *Children of Albert B. (III, 14, normal).*

IV, 34. Mrs. Sn, of Wandsworth. Aged 26. Reputed normal.
IV, 35. Marjorie B. Aged 22. Reputed normal.
IV, 36. Edna B. Aged 18. Reputed normal.

(10) *Children of Mrs. Florence D. (III, 15, normal).*

IV, 37. Female. Aged 28. Examined, normal.
IV, 38. Male. Killed aged 9. Reputed normal.

(11) *Children of Mrs. Hl (III, 16, normal).*

IV, 39. Female. Aged 25.
IV, 40. Female. Aged 21.
} Reputed normal.

(12) *Children of Henry B. (III, 17, affected).*

IV, 41. Male. Aged 21. Reputed normal.
IV, 42. Male. Aged 5½. Examined at Royal Eye Hospital. Normal.

(13) *Children of Mr. Bt (III, 21, normal).*

IV, 43. Mrs. E., of Chesham. Aged 42. Reputed normal.
IV, 44. Male. Died age 22. Reputed normal.
IV, 45. Miss Bt, of Chesham. Aged 37. Reputed normal.

(14) *Child of Mr. Lt (III, 22, normal).*

IV, 46. Female, of U.S.A. Aged 26. Reputed normal.

Generation V.

(1) *Child of Mrs. U. (IV, 1, normal).*

V, 1. Female. Aged 29. Reputed normal.

(2) *Children of Harry Br (IV, 4, affected).*

V, 2. Brenda Br. Aged 15. Examined, normal.
V, 3. Christine Br. Aged 10. Examined, normal.

(3) *Children of Mrs. Rl (IV, 5, normal).*

V, 4. Female. Aged 27.
V, 5. Female. Aged 25, approximately.
V, 6. Male. Aged 11.
V, 7. Female. Aged 8.
} Reputed normal.

(4) *Children of Mrs. M. (IV, 6, normal).*

V, 8. Male. Aged 18. Reputed normal.
V, 9. Female. Aged 13. Reputed normal.

(5) *Children of George Br (IV, 7, normal).*

V, 10. Male. Aged 14.
V, 11. Male. Aged 10.
V, 12. Female. Aged 2.
} Examined, normal.

(6) *Child of Mrs. Bl (IV, 9, normal).*

V, 13. Male. Aged 29. Reputed normal.

(7) *Child of Mrs. Hy, junior (IV, 11, normal).*

V, 14. Male. Aged 26. Examined, normal.

(8) *Child of Leonard B. (IV, 12, normal).*

V, 15. Male. Killed aged 19. Reputed normal.

(9) *Children of Sidney B. (IV, 13, normal).*

V, 16. Female. Aged 6. Examined, normal.
V, 17. Male. Aged 3. Examined, normal.

(10) *Child of Jack Hy (IV, 14, normal).*

V, 18. Tony Hy. Aged 12. Examined, normal.

(11) *Children of Mrs. Ws (IV, 15, normal).*

V, 19. Joyce Ws. Aged 20.
V, 20. June Ws. Aged 18.
V, 21. Keith Ws. Aged 17.
} Reputed normal.

(12) *Children of Mrs. Rd (IV, 16, normal).*

V, 22. Peter Rd. Aged 14. Examined, normal.
V, 23. Gillian Rd. Aged 6. Examined, normal.
V, 24. Pauline Rd. Aged 3. Reputed normal.

(13) *Child of Dennis Hy (IV, 17, normal).*

V, 25. David Hy. Aged 2½. Reputed normal.

(14) *Children of Mrs. He (IV, 25, normal).*

V, 26. John He. Aged 8. Examined, normal.
V, 27. Female. Reputed normal.

(15) *Children of Mrs. Mr (IV, 27, normal).*

V, 28. Female. Aged 3½
V, 29. Male. Aged 18 months.
} Reputed normal.

(16) *Child of Cecil B. (IV, 28, normal).*

V, 30. Female. Aged 14 months. Reputed normal.

Generation VI.

Children of V, 1. (female, normal).

VI, 1. Male. Reputed normal.
VI, 2. Female. Reputed normal.

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THE OPHTHALMOSCOPICAL APPEARANCE OF THE FUNDUS OCULI IN ELDERLY PERSONS WITH ARTERIO-SCLEROSIS AND NORMAL BLOOD PRESSURES*

BY

H. VOGELIUS AND P. BECHGAARD

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IN considering the pathological changes in the retinal vessels it is important to know which changes are due to arterio-sclerosis and which to hypertension. On this question there is, however, considerable uncertainty.

Berglund (1945) has reviewed the literature and criticizes the usual accepted classification.

Kornerup (1947), who gives an excellent review of the literature, assumes purely hypertensive changes to be present when the arteries show increased fullness and an exaggerated reflex streak and slight vestiges of crossing phenomena, " indentations ". The localized and general narrowings of the arteries have been assumed to be of spastic origin, if they are reversible, and if the vessels in the narrowed parts have normal transparency and no other signs of thickening of the walls. He assumes arterio-sclerosis to be present when the calibre of the artery is distinctly and irreversibly reduced, locally or generally, especially when the arteries have lost their transparency. All kinds of well-marked crossing-phenomena, especially those where the artery is opaque, further, tortuosity of the perimacular vessels and sheathing of the vessels of the 2nd and 3rd order, have each one separately and still more all together been assumed to indicate arteriosclerosis.

Elwyn (1944) regards the following appearances as characteristic of hypertensive retinopathy :

(1) Oedema of retina and papilla.
(2) " Cotton wool exudates ".
(3) Haemorrhages.
(4) Sharply defined white spots in the deeper layers of the retina.
(5) Stellate macula.

Wagener (1939) regards the following as characteristic of arterio-sclerosis :

(1) Even constriction of the vascular lumen, without changes in calibre.
(2) Alteration of the vascular reflex.
(3) Arterio-venous compression.
(4) Localized spasms—irregularities of calibre.
(5) Peri-arterial sheathing.

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Gans (1944) says that hypertensive and arterio-sclerotic changes are usually present together, and uses the following classification (A : arterio-sclerosis; H : hypertension):

A_oH_o.	Normal.
A_I.	Slight arterio-sclerosis.
A_{II}.	Severe arterio-sclerosis with signs of local circulatory insufficiency.
A_{III}.	Severe arterio-sclerosis.
H_I.	Constriction of the arterioles.
H_{II}.	Hypertensive retinopathy.
H_{III}.	Hypertensive retinopathy—papilloedema.

The classifications of Gans and Wagener differ in that Gans regards the constrictions of the arterioles (spasms) as hypertensive, and Wagener regards them as arterio-sclerotic. Gans does not point out which signs he believes to be characteristic of arterio-sclerosis and which of hypertension.

Woods and Peet (1941) have classified cases of hypertensive retinopathy according to their severity; in this grouping the significance of spasms is stressed:

Group 1. Normal ophthalmoscopic appearance.
Group 2. Arterio-sclerosis without spasms.
Group 3. Definite spasms with or without irregularities of calibre, with or without haemorrhages or exudates.

The classification of retinal changes in hypertension which is most used at the present time is that suggested by Wagener and Keith (1937):

Group 1. Slight constriction of the arteries or slight arterio-sclerosis.
Group 2. More marked constriction of the arteries or more marked arterio-sclerosis.
Group 3. The same plus exudates and haemorrhages.
Group 4. The same plus papilloedema.

The classifications of Woods and Peet, and of Wagener and Keith, do not deal with the differential diagnosis between hypertensive and arterio-sclerotic changes.

When we were studying the retinal changes in hypertension we could find in the literature no account of the appearance of the retina in the older age-groups based on a large group of persons with normal blood pressures. As such an account seems essential if one is to distinguish between hypertensive and arterio-sclerotic changes, the appearance of the retina of elderly persons with normal blood pressures is described here.

Material

124 subjects (85 men and 39 women) with normal blood pressures, as confirmed by repeated recordings, have been examined. The blood pressures were below 140 mm. Hg. systolic and 90 mm. Hg. diastolic. The ages varied from 40 to 95 years, 25 in each 10-year group, except in the last in which there were only three persons over 90 years of age. The subjects over the age of 65 years were chosen from the old people's home; all of them had clinical signs of arterio-

sclerosis. Those under 65 years were either normal subjects or patients from the Copenhagen Municipal Hospital suffering from conditions not affecting the vascular system.

Method

The ophthalmoscopic examinations were all made by one ophthalmologist; mydriasis was used in all cases.

Particular attention was paid to the following: arterial diameter (including irregularities of calibre and spasms), arterio-venous crossings, course and reflex of the arteries.

The condition of the veins and retina was also studied, the latter with special attention to haemorrhages, exudates, thromboses, and the papilla.

The results appear in the Table opposite.

Results

Arteries.—Changes probably due to arterio-sclerosis (abnormal arterio-venous crossings, the veins being slightly depressed, raised, or displaced sideways) were seen even in the youngest age-group (40-50 years). Slight irregularities of calibre were also seen in this group, but constriction of the arteries was seen in only one case under 60 years. The frequency of abnormal arterial diameters (narrowed or irregular) and of abnormal arterio-venous crossings increases rapidly at 60 years and continues to increase with age. Irregularities of calibre were found in all the 49 cases of over 70 years of age. The frequency of abnormal reflex also increases with age.

In only three out of the 124 cases was the course of the arteries abnormally tortuous. It must however be emphasized that the opinion whether an artery is tortuous or not is purely subjective, and cannot be assessed objectively like arterial constriction or irregularities of calibre.

Compression of the vein with peripheral dilatation and tapering towards the artery was seen in only two cases. Spasms (temporary or permanent marked constrictions of varying lengths along an otherwise normal artery) were not seen.

Veins.—Nothing notable. It may be mentioned that no thromboses were seen.

Retina.—Haemorrhages, exudates, blurred disk edges, or papilloedema were not seen. In the older age groups some pale disks and various changes in the macula were recorded, but they were not associated with any decrease in visual acuity. Only five of the 124 subjects had a visual acuity below 6/18 with proper correction.

Summary

The fundus oculi of 124 persons over 40 years of age with normal blood pressures, and in many cases with marked arterio-sclerosis, have been examined ophthalmoscopically. Changes in the retinal

TABLE

Findings in the Fundus Oculi of 124 Elderly Persons with Normal Blood Pressures

Age-group		40–49	50–59	60–69	70–79	80+
No. of patients		26	25	24	25	24
Visual acuity < 6/18		0	0	1	1	3
Pale disk		1	0	2	4	11
Arteries	Narrow	0	1	8	12	12
	Very narrow	0	0	1	1	6
Irregularities of calibre	Slight	3	9	12	14	15
	Marked	0	0	6	11	9
Spasms		0	0	0	0	0
Abnormal reflex		0	4	15	22	23
Abnormal arterial tortuosity		0	0	1	0	2
Abnormal veins		0	0	0	0	0
Venous depressions	Slight	4	6	11	9	12
	Definite	0	0	1	1	0
Abnormal fovea		0	0	5	12	17
Haemorrhages		0	0	0	0	0
Thrombosis		0	0	0	0	0
Exudates		0	0	0	0	0
Papilloedema		0	0	0	0	0

arteries (slight irregularities of calibre, and slight changes at the arterio-venous crossings) were found in a few cases in the 40-50 years age group. Over the age of 60 years these changes increased in degree and frequency, and many constricted arteries were found.

These two types of change correspond with the alterations occurring in patients with hypertension in Wagener and Keith's Groups 1 and 2.

Spasms of the arteries and retinopathy were not seen.

We should like to express our thanks to chief physician T. Geill, M.D. for permission to examine his patients.

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BOOK NOTICE

Amsler Charts. Published by Hamblin, London, 1950. Pp. 12, with the 7 charts in Loose-leaf book. Price 37/6.

Most British ophthalmologists will be familiar with the methods of qualitative analysis of the central visual field elaborated and introduced by Professor Marc Amsler of Zürich. The main chart of Amsler's system consists of a grid of 400 squares ruled in white on a black background, with a white fixation spot in the centre; the grid is so arranged that when held 28-30 cm. from the eye, the sides of the whole pattern of squares subtend angles of 20°, and each small square an angle of 1° at the nodal point. The network therefore, on the retina, would occupy, when the central point is fixed, an area of 10° all round the fixation point, thus covering the whole macular area but not extending out temporally as far as the blind spot. This chart with various modifications of the primary pattern affords a rapid, and apparently accurate, method of analysing subjectively the visual disturbances which accompany the beginning and evolution of macular disturbances. These are mapped out by the patient as areas of disappearance, distortion, etc., of the grid pattern, findings which can be drawn on the duplicate pad of charts supplied in the book.

The method, of which we have some experience, is of considerable value in routine clinical work, and ophthalmologists should welcome the opportunity of obtaining the charts, with full and explicit instructions for their use, in a convenient loose-leaf form.

OPHTHALMOLOGICAL INVESTIGATIONS OF 500 PERSONS WITH HYPERTENSION OF LONG DURATION*

BY

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FOR many years it has been an established fact that severe changes in the retina, *i.e.*, haemorrhages, exudates, and papilloedema (" retinitis albuminurica ") indicate a bad prognosis in patients suffering from hypertension, but the slighter changes have only attracted attention during recent years.

Wagener and Keith (1939) proposed a classification of hypertension into four groups according to the changes in the retina. This classification has many supporters amongst both ophthalmologists and physicians, although their first two groups were based on only 36 patients, whereas Groups 3 and 4 contained 180 patients. Their material appears, in fact, to have been very selected; it consisted almost entirely of patients with the most severe degrees of hypertension, many having nephrosclerosis or malignant hypertension.

Undoubtedly, as the authors themselves stressed, this material gives a false impression of the frequency of the different degrees of retinal changes in hypertension. Bechgaard has shown that malignant hypertension probably does not make up more than 1 per cent. of all cases with this condition. Wagener and Keith's work on the ophthalmoscopic appearances in patients with hypertension aroused considerable interest, and it was expected that pathological changes in the retina would be present in a large number of the patients.

However, retinal changes can only be found with similar frequency in hospitals and clinics where a large number of true malignant cases of hypertension are investigated. It is therefore interesting to determine the frequency with which retinal changes appear in more representative series of cases with hypertension.

It would have been particularly interesting, if our cases had also been investigated ophthalmoscopically, when the hypertension was first diagnosed, but only patients with hypertension of long duration have been studied here. Therefore malignant cases and cases of short duration are automatically excluded. In this respect the material differs entirely from that of Wagener and

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Keith and may be regarded as a supplement to their investigations. For references to the literature refer to Wagener and Keith (1939), and Duke-Elder (1940).

Material and Methods of Investigation

Bechgaard has examined 1,038 out-patient cases of hypertension (325 men and 713 women). At their first examination, from 4 to 11 years earlier, all had had a blood pressure of at least 160/100 mm. Hg or a systolic blood pressure of at least 180 mm. Hg. 485 were re-examined ophthalmologically by Porsaa at the Ophthalmological Department of the Rigshospital. These were all patients who attended the clinic for investigation; patients examined in their homes did not have the supplementary ophthalmic examination. About 97 per cent. of all surviving patients were re-examined; 293 (133 men and 160 women) had died during the observation period.

The different patients were all examined by the same ophthalmologist. The investigation comprised estimation of visual acuity and refraction, examination of the refracting system, and an ophthalmoscopic examination during mydriasis to allow the vessels to be followed to the periphery. The condition of the fundi (arterial diameter, course of the arteries, arterial reflex, arterio-venous crossings, appearance and localization of haemorrhages, presence and appearance of exudates, and condition of the fovea) was described systematically to secure that the examination was as uniform and comprehensive as possible. The ophthalmologist was not informed of the patient's blood pressure before the examination.

In 45 patients other ophthalmological conditions prevented an exact description of the fundi. These were: nystagmus (2), corneal opacity (3), glaucoma (3), high myopia (4), cataract (26), severe astigmatism (2), atrophy of the optic nerve (2), and diabetic retinopathy (1).

Medical Investigation. The material is divided into Wagener and Keith's four groups. It is not clear whether their Group I included cases of hypertension without any vascular changes as well as those with slight changes. Their paper did not contain a Group 0, but like other later investigators we have found it necessary to include such a group for the cases without any vascular changes. The patients in each group are also graded according to their symptoms, which were as follows: headache (44), vertigo (53), nervousness (93), cardiac pain (48), palpitations (60), dyspnoea (56), hot flushes (56), epistaxis (5), previous cerebral haemorrhage (0).

Grade A: no symptoms.
Grade B: slight symptoms.
Grade C: inconvenienced by their symptoms.
Grade D: incapacitated by their symptoms.

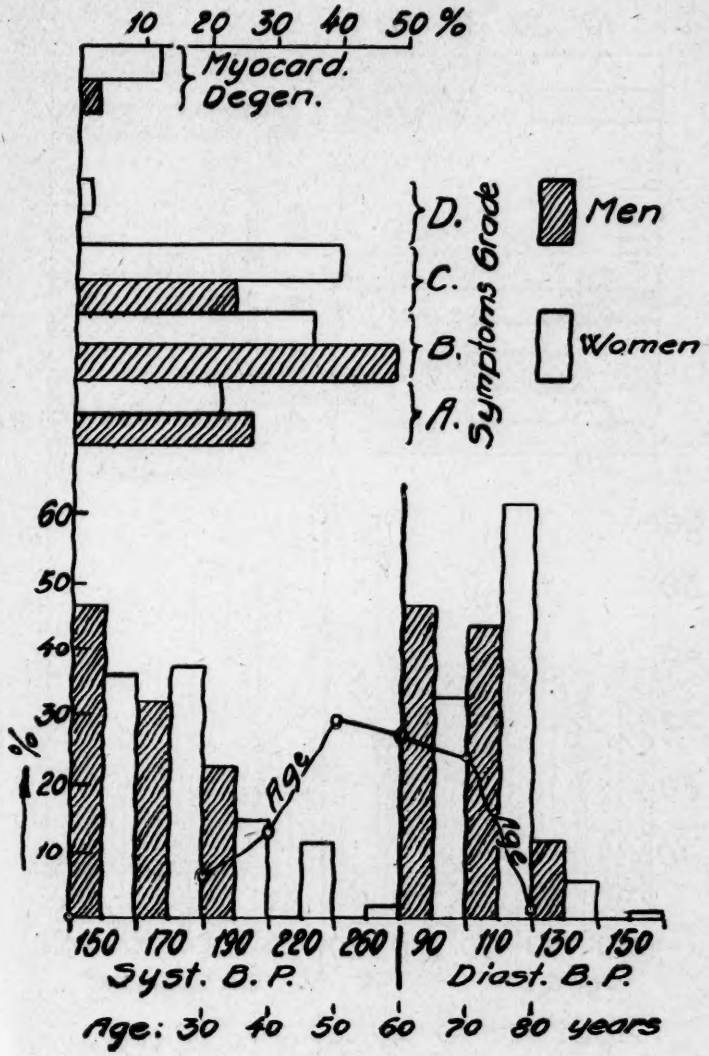

FIG. 1.—Group 0. No vascular changes in fundus.

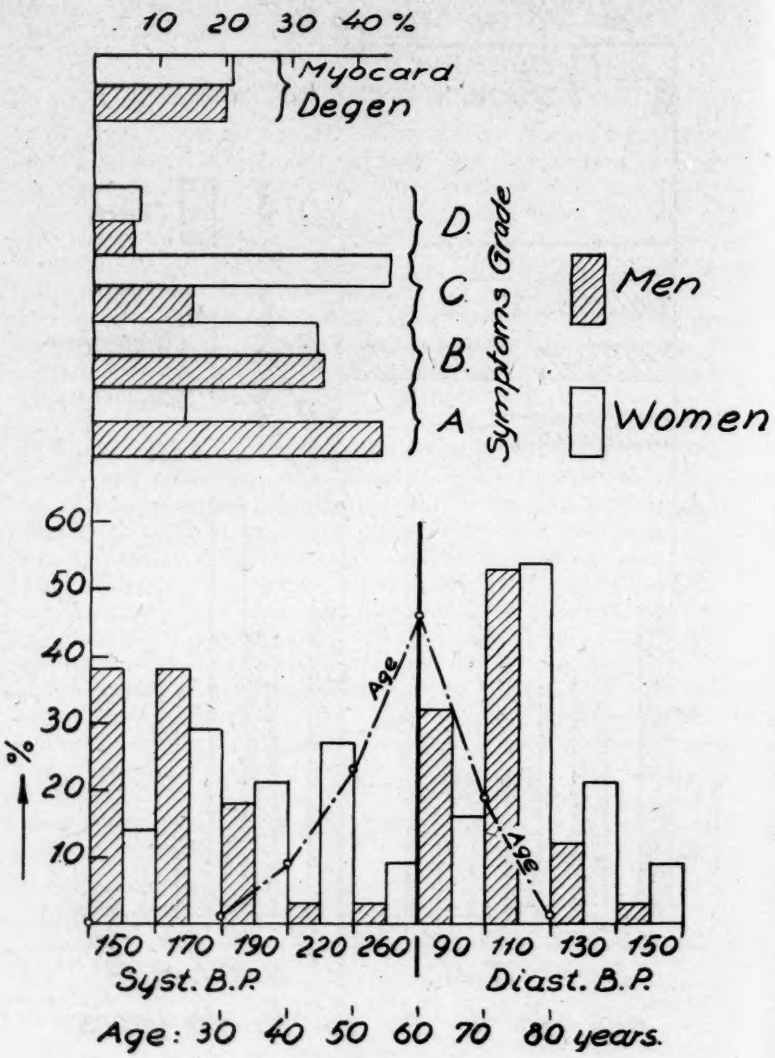

FIG. 2.—Group 1. Slight constriction and sclerosis of the arteries.

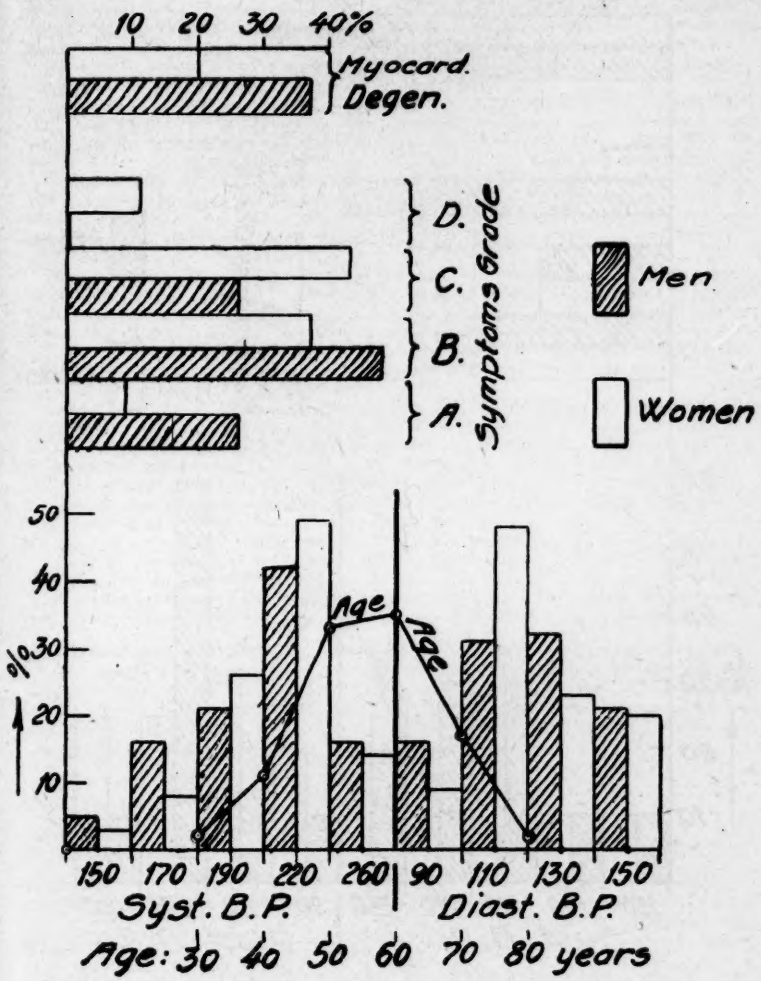

FIG. 3.—Group 2. More pronounced changes in fundus.

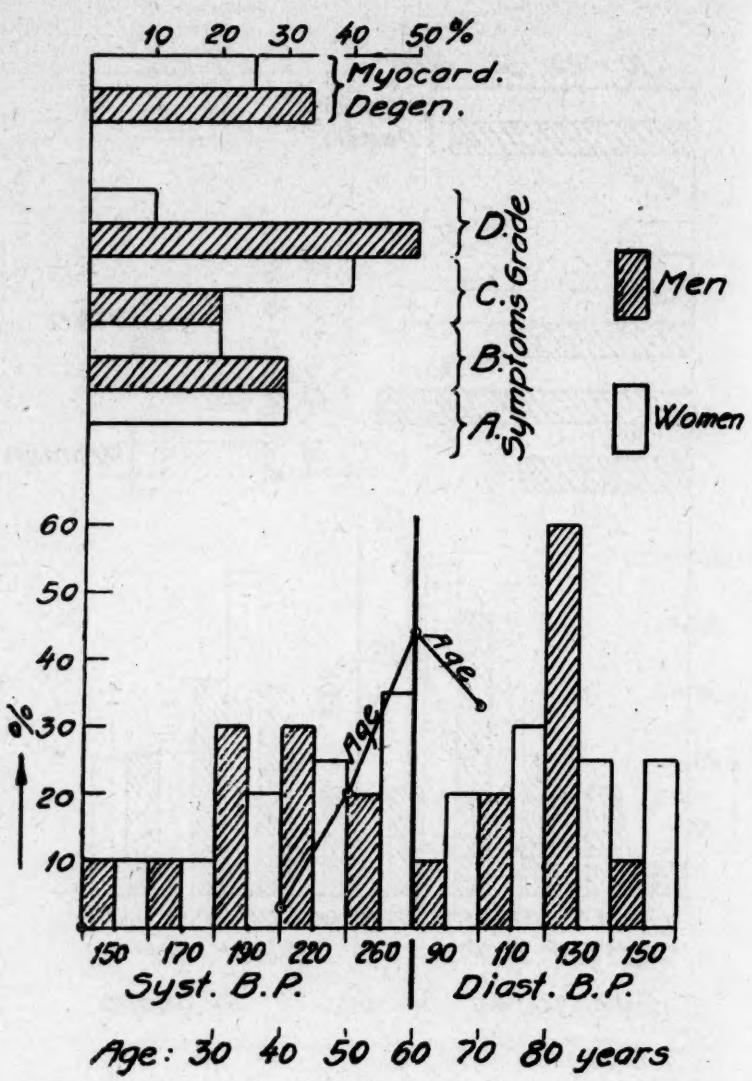

FIG. 4. Group 3. Haemorrhages or exudates in addition to other vascular changes.

Group 0 (Fig. 1), no vascular changes in fundus, contains 160 patients (37 men, 123 women). The average age is the same for men and women, but the blood pressure of the women is somewhat higher (both systolic and diastolic). In this group the blood pressure is often only slightly raised. The women are more affected by hypertension, and myocardial degeneration is more frequent.

No man in Group 0 had a systolic blood pressure over 200 mm. Hg or a diastolic pressure over 140 mm. Hg.

It is noteworthy that there were 160 patients known to have had hypertension for 10 or more years in whom no retinal vascular changes could be detected even with careful ophthalmic examination. The fact that so many cases had no vascular changes in the fundus seems to us one of the most interesting findings.

Group 1 (Fig. 2), slight constriction and slight sclerosis of the arteries, contains 179 patients (34 men, 145 women). Compared with the patients in Group 0, those in Group 1 are older, they have somewhat higher systolic and diastolic pressures, and their symptoms—especially those of myocardial degeneration—are more frequent.

Group 2 (Fig. 3), more pronounced changes, the arteries are more constricted or more sclerotic, contains 54 patients (19 men, 35 women). The average age for men and women is almost the same, and the patients are on an average a little older than those in Group 1. The blood pressures are considerably higher, and are the same for men and women. The frequency of myocardial degeneration amongst the men of this group is twice that in Group 1. There is no marked increase in symptoms.

Group 3 (Fig. 4), haemorrhages or exudates in addition to other vascular changes but no papilloedema, contains only thirty patients (10 men, 20 women); cases of diabetes and branch-thrombosis have been excluded. The average age is somewhat higher than in Group 2, the distribution of blood pressure the same. In this group the men are more inconvenienced by their symptoms. The frequency of myocardial degeneration is not higher than in Group 2, and it is remarkable that 75 per cent. of the women and 66 per cent. of the men show no sign of myocardial degeneration in spite of the severe retinal changes.

Group 4, papilloedema in addition to haemorrhages and exudates, contains only one case. This fact corresponds with our general view that in an average cross-section of hypertensive patients cases of malignant hypertension are extremely rare, since it most often appears as a relatively acute disease in middle age.

Ophthalmological Investigation.—In addition to papilloedema the condition of the vessels and the presence of exudates and haemorrhages are the facts of special interest in the investigation of the fundi in hypertension. The condition of the arteries may be ascertained from their diameter, the arterio-venous crossings, the course of the arteries, and the arterial reflex. The scheme needed for assessing the arterial diameter is shown in Table I.

TABLE I

Retinal Arteries in Hypertension

Condition of Arteries	Men		Women		Total	
	Number	%	Number	%	Number	%
Normal	72	68	219	66	291	66
Narrow	27	25	77	23	104	24
Very narrow	13	12	31	9	44	10
Isolated spasms	5	5	25	8	30	7
Greater areas of arterial spasm ...	3	3	9	3	12	3
Obliterated arteries	2	2	2	1	4	1
Slight irregularities in calibre ...	18	17	71	21	89	20
Severe irregularities in calibre ...	15	14	14	4	29	7

Diameter of the Arteries.—The estimation of the size of the arteries depends on a general judgment (relation to the size of the veins), but it must be pointed out that *all* the examinations were performed by the same ophthalmologist. No measurements were recorded, as it is impossible to obtain a correct figure, and they are therefore of no value, as they cannot be compared with the standard diameters. The findings are shown in Fig. 5 relation to the patient's age, systolic and diastolic blood pressures, and general health. The ordinate indicates the percentage of cases with abnormal arterial diameters, and it is clear from the table that there is a positive correlation between the increase in blood pressure and the number of abnormal arterial diameters; this is most pronounced in relation to the diastolic blood pressure.

There is no correlation between the age and the abnormalities, the record is almost horizontal, and abnormalities are almost constant at about 35 per cent.

Irregular calibre was seen in 27 per cent. of the older patients, usually after the age of 60 years, and in 50 per cent. of these cases the systolic blood pressure

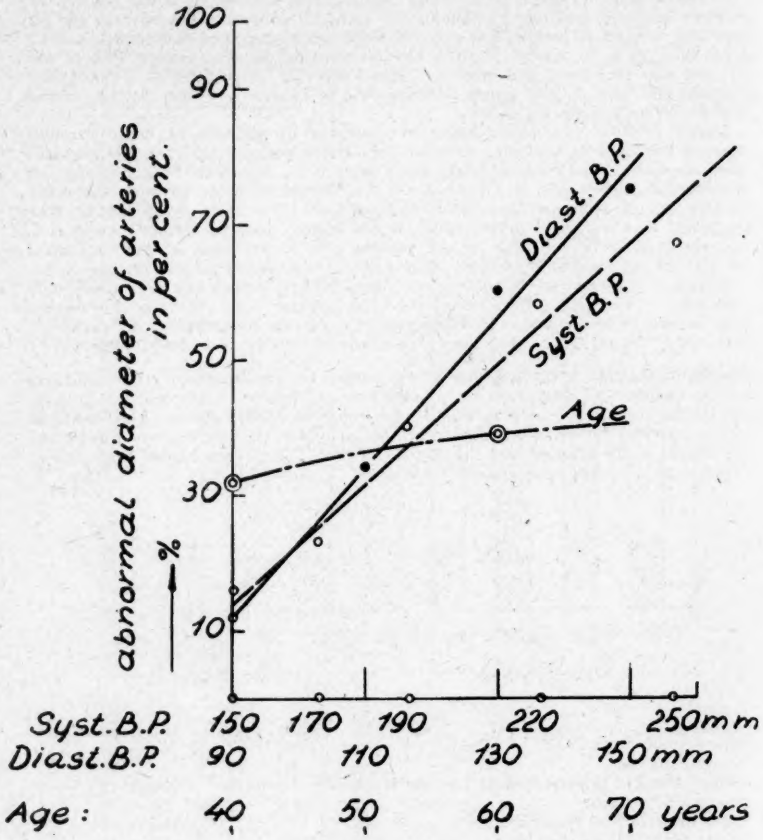

FIG. 5.—Diameter of the arteries.

was less than 200 mm. Hg; the diastolic blood pressure was also of no significance for the frequency of the irregularities in calibre.

Spasms were most frequently found in the younger individuals at systolic blood pressures exceeding 200 mm. Hg or diastolic exceeding 110 mm. Hg. Spasms were relatively rare, occurring in only 10 per cent. of the cases (6 per cent. had systolic blood pressures over 200 mm. Hg).

The relation between the general condition of health and abnormal arterial diameter has also been recorded, and it appears that in Grades A, B, and C, the number of patients with normal arterial diameters is twice those with abnormal diameters. Only in Grade D was there a slight predominance of abnormal diameters.

Arterio-Venous Crossings.—(Table II) Fig. 6 suggests that there is a considerable positive correlation between the increasing blood pressure (especially the diastolic blood pressure) and the number of cases with abnormal arterio-venous crossings. Further it can be seen that over 50 years of age there is no relation between the

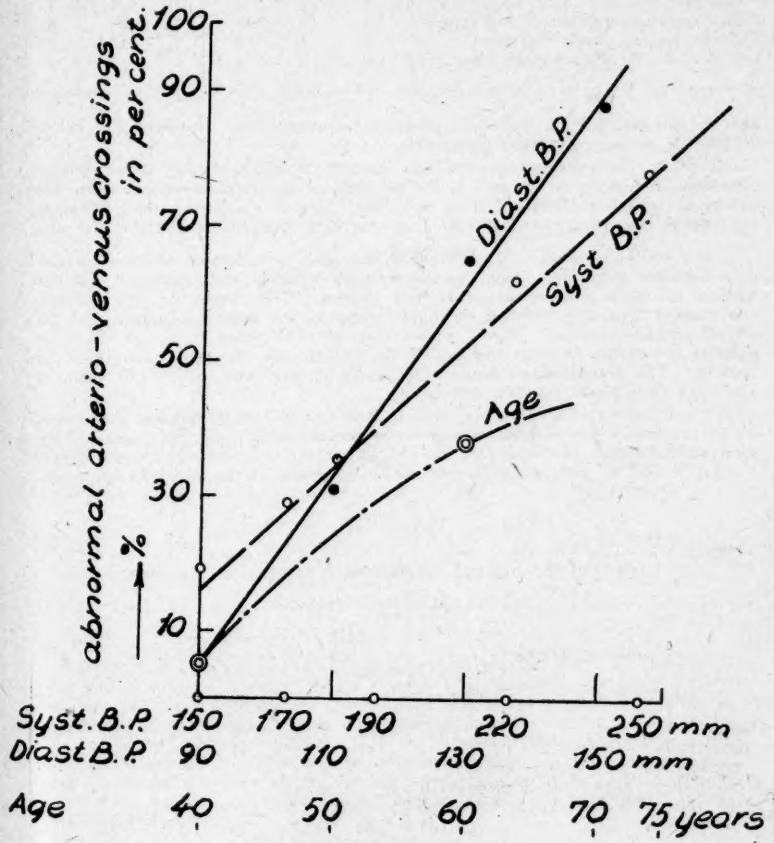

FIG. 6.—Arterio-venous crossings.

TABLE II

Arterio-Venous Crossings in Hypertension

Condition of Crossings	Men		Women		Total	
	Number	%	Number	%	Number	%
Normal	73	68	205	62	278	63
Depression of vein	25	23	87	26	112	25
Sideways displacement of vein ...	10	9	35	11	45	10
Arched elevation of vein	12	10	35	11	47	10
Venous compression with peripheral dilation	1	1	3	1	4	1
Vein concealed on either side of artery	15	14	24	7	39	9
Tapering of vein towards artery ...	4	4	7	2	11	2
Common sheath of vein and artery	0	0	1	1	1	1

age and the number of cases with abnormal arterio-venous crossings, but below 50 there is perhaps a positive correlation.

Regarding the relation between the general health and the arterio-venous crossings, in Grades A, B, and C the number of normal crossings is twice the abnormal, while in Grade D there are four times as many abnormal crossings as normal. Severe compression of the vein with peripheral dilatation is rare.

Course of the Arteries.—(Table III) There is a considerable positive correlation between increasing blood pressures, both systolic and diastolic, and the number of cases with abnormal arterial courses. The correlation is, however, less marked than that between the blood pressure, the arterial diameter, and the arterio-venous crossings. Fig. 7 shows that over 50 years of age there is no positive correlation between the age of the patient and abnormal courses of the arteries. The abnormalities amount to about 30 per cent.; under 50 years of age there is a slight positive correlation.

The soft curves of the arteries seem to have the closest correlation with raised blood pressure. The relation between the general health and the course of the arteries shows that in Grades A, B, and C contain twice as many cases with a normal course as with an abnormal, while in Grade D the numbers are equal.

TABLE III

Course of the Retinal Arteries in Hypertensive Subjects

Course of Arteries	Men		Women		Total	
	Number	%	Number	%	Number	%
Normal	83	78	256	76	339	78
Abnormally tortuous	11	10	47	14	58	13
Very tortuous with typical soft curves, as if artery is too long in proportion to vein with rectangular crossings of veins	22	21	38	11	60	14

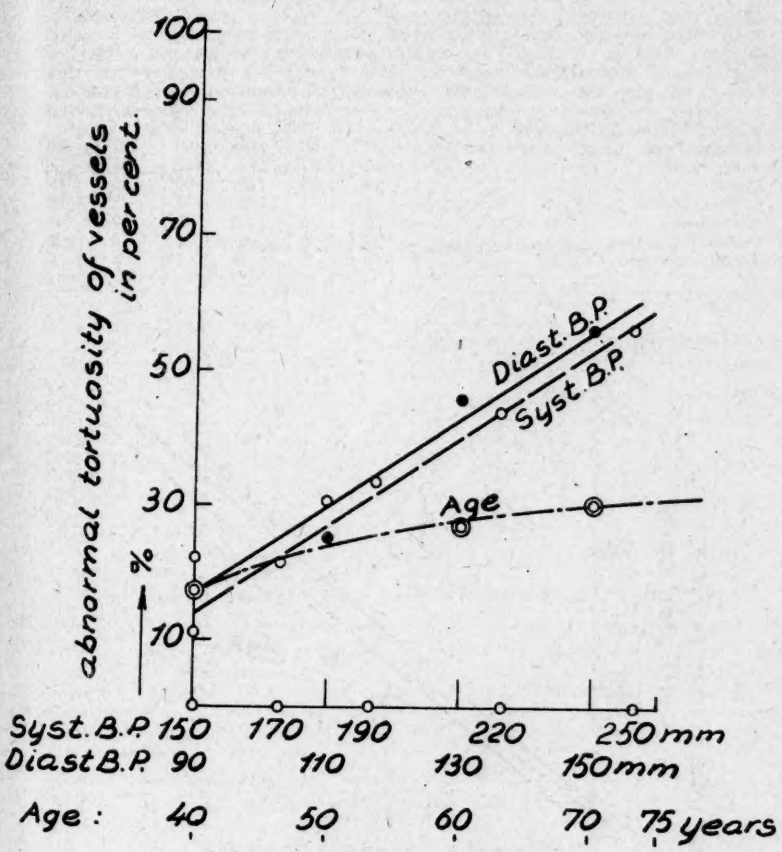

FIG. 7.—Course of the arteries.

Arterial Reflex.—(Table IV) It appears that copper-wire and sheathing are rare, and silver-wire arteries do not occur. Fig. 8 shows a positive correlation between the blood pressure and the number of cases with abnormal reflex, as in the course of the arteries. The lines have practically the same slope as those for the course of the arteries, but they are displaced upwards, showing a higher average percentage of abnormality. The meaning of this displacement is, however, doubtful. Over 50 years of age there seems to be no positive correlation between the arterial reflex and the age of the patient; the abnormalities amount to about 50 per cent.

TABLE IV

Arterial Reflex in Hypertensive Subjects

Arterial Reflex	Men		Women		Total	
	Number	%	Number	%	Number	%
Normal	70	65	167	50	237	54
Sharp, light	40	37	151	45	191	43
Broad	36	34	122	37	158	36
Copper-wire	6	6	2	1	8	2
Silver-wire	0	0	0	0	0	0
Partially sheathed	3	3	5	2	8	2
Totally sheathed	2	2	1	1	3	1

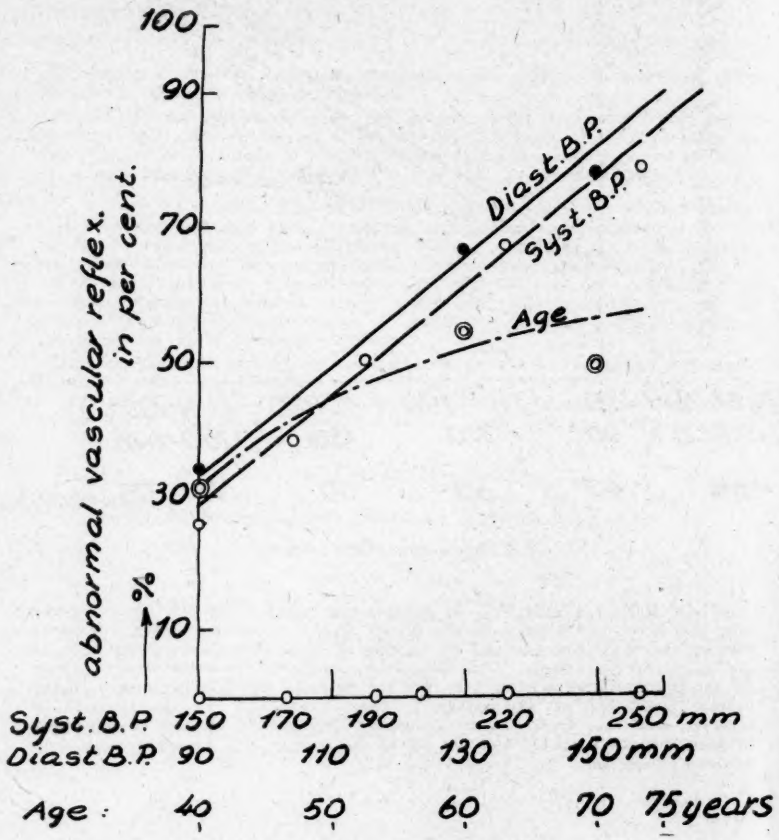

FIG. 8.—Arterial reflex.

Retinal Veins.—The condition of these veins is recorded in Table V.

Pulsation in the Central Vein.—The frequency of spontaneous pulsation in the central vein is as shown in Table VI.

Pathological Changes.—Very few haemorrhages and exudates were found; Group 3 contained only thirty cases, though patients with only one haemorrhage or patch of exudate were included in this group. This figure is small compared with that of Wagener and Keith. Group 4 contained one case with blurred disks; papilloedema was not seen. In the whole material there was only one patient in Wagener and Keith's Group 4.

Visual Acuity.—(Table VII) 91 per cent. of all cases had a visual acuity of 6/12 or over. Visual acuity of 6/18 or below was due to central chorioretinitis; it was present in ten men and 24 women.

TABLE V

Retinal Veins in Hypertensive Subjects

Retinal Veins	Men		Women		Total	
	Number	%	Number	%	Number	%
Normal	90	84	292	88	382	87
Dilated	6	6	7	2	13	3
Dark	10	9	12	4	22	5
Tortuous	10	9	17	5	27	6
Sheathed	2	2	0	0	2	1
Thrombosed	2	2	4	1	6	1

TABLE VI

Pulsation in the Central Vein in Hypertensive Subjects

Pulsation	Men		Women		Total	
	Number	%	Number	%	Number	%
Spontaneous	93	87	304	91	397	90
Non-spontaneous	14	13	29	9	43	10

TABLE VII

Percentage Distribution of Visual Acuity

Acuity	6/6	6/9	6/12	6/18–6/24	6/36–6/60	< 6/60
Percentage	79	8	4	5	1	3

Discussion

The severest retinal changes are scarcely represented. Blurred disk edges were found in only one, and haemorrhages and exudates in only thirty cases.

The objects of this investigation were to establish the frequency of the various vascular changes in the retina in the common form of hypertension of long duration; to correlate the relation of these changes to the blood pressure and the age; and to gain an impression of which changes have the greatest diagnostic value. The condition of the veins gives little information, so interest is focused mainly on the arteries.

Arterial Diameters.—Normal diameters were found in 50 per cent. of the patients, narrow or very narrow arteries in 34 per cent., irregularities of calibre in 27 per cent—seen usually in older people with relatively low blood pressures. Spasms were seen in only 10 per cent., mostly young patients with higher blood pressures.

Arterio-Venous Crossings.—These were normal in 63 per cent.; in the remaining 37 per cent. the vein was found depressed; real compression, however, was rare (seen in four patients, 1 per cent.).

Course of the Arteries.—This was normal in 72 per cent.; amongst the abnormal the typical soft curves were most closely related to the increased blood pressure.

Arterial Reflex.—This was normal in 54 per cent.; in the remaining 46 per cent. the reflex deviated from the normal, but copper-wire arteries and sheathing were only found in 4 per cent. There were no silver-wire arteries.

Pathological Changes.—These conditions in the retinal vessels in hypertension are of much less importance than is generally believed. The retinal vessels were still normal after many years of hypertension in 38 per cent., and in 42 per cent. they showed only slight changes (Wagener and Keith's Group 1). Severe changes without retinopathy were seen in 13 per cent. (Wagener and Keith's Group 2), and only 7 per cent. of the cases had retinopathy (Wagener and Keith's Groups 3 and 4). Apart from exudate and papilloedema there was little correlation between the condition of retinal vessels and the general clinical condition. Amongst the patients in Group 0, with normal retinae, were many both with considerable symptoms from their hypertension and with hypertensive cardiac disease, and in Groups 2 and 3 many patients had no symptoms from their hypertension and showed no signs of cardiac disease.

Vogelius and Bechgaard are publishing in this issue the results of the examination of the fundi in 124 elderly persons with normal blood pressures, which they made in order to gain an impression of which facts might be of use for the differentiation between purely hypertensive, and purely arterio-sclerotic changes in the retina. Apart from haemorrhages, exudates, papilloedema, and spasms, which were not found in this control material, the same types of changes were found as in the patients with hypertension. There was only one difference, that vascular changes were found in patients with hypertension at an earlier age.

Further, it might be stressed that in hypertension the characteristic abnormality of the arteries is usually their narrow diameter, while in arterio-sclerosis it is their irregularity.

It seems that the effect of the hypertension on the retinal vessels, at any rate as far as the slighter changes are concerned, is primarily an acceleration of the arterio-sclerosis which often develops without hypertension at a later age (between 55 and

60 years). Consequently, the presence of such changes, especially spasms and narrow arteries, below 55 years suggests hypertension; on the other hand the absence of retinal changes does not exclude even an advanced stage of hypertension.

The fact that there is a positive correlation between the blood pressure, both systolic and diastolic, and the appearance of vascular changes in the retina, cannot be ignored, but a slight correlation with the age can also be demonstrated. Both the degree and frequency of the vascular changes increase with the age of the patient in both the control material and the patients with hypertension, but this increase is more rapid in the control material. This fact is difficult to explain.

Wagener and Keith's system of four groups has contributed most valuably to the description of the different degrees and forms of retinal changes and has provided a clear nomenclature. It has also been helpful in the medical assessment of the condition of the patients with hypertension. It cannot, however, be recommended as the main medical classification and sole prognostic guide in hypertension, as has been the tendency in recent years. The changes in the retina are only a sign, like many others in hypertension, and, excepting the relatively rare exudates and papilloedema, they are much less significant for prognosis than, for example, the condition of the myocardium. As mentioned in the introduction only Wagener and Keith's Groups 3 and 4 are based on a sufficient number of patients to justify a prognostic conclusion, so that this classification appears to have little prognostic value in the less severe groups. In most cases of hypertension the condition of the retina alone is useless as a prognostic indicator. As has been stressed by Rogers and Palmer (1947), Peet and Isberg (1946), and Hammarström and Bechgaard (1950), the changes in the heart, kidneys, and brain, and the age and sex of the patient, which appear to have been ignored in previous works, must also be taken into consideration.

Summary

(1) 485 hypertensive persons were examined medically and ophthalmologically 4 to 11 years after the hypertension had first been detected.

(2) The retinal vessels were normal in 160.

(3) The most severe retinal changes were scarcely seen. Only one case with blurring of the disk edge and thirty cases with haemorrhages and exudates were found.

(4) The arterial diameters were normal in 50 per cent. of the patients, narrow, or very narrow in 34 per cent. and irregular in 27 per cent.

(5) The arterio-venous crossings were normal in 63 per cent., in the remaining 37 per cent. the vein was found to be depressed, but real compression was rare.

(6) The course of the arteries was " normal " in 72 per cent. Amongst abnormalities the typical soft curves are most closely related to the raised blood pressure.

(7) The arterial reflex was normal in 54 per cent. The remaining 46 per cent. had reflexes deviating from the normal. Copper wire arteries and sheathing were only found in 4 per cent. There were no silver-wire arteries.

(8) When the cases were classified according to Wagener and Keith's classification no convincing correlation between the degree of change in the retinal vessels and the condition of the patient was found. Quite normal fundi were often found after many years' severe hypertension in persons who were severely affected by their hypertension, and who had signs of myocardial damage, while there were definite changes in the retinal vessels in many cases with no symptoms and a normal electrocardiogram.

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EXPERIMENTAL STUDY ON THE EFFICIENCY OF DIFFERENT SUBSTANCES IN RETARDING THE ABSORPTION OF PENICILLIN INTRODUCED INTO THE SUBCONJUNCTIVAL SPACES*

BY

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THERE is no doubt that therapeutic levels of penicillin can be obtained in the aqueous and the tissues of the anterior segment of the globe, by injecting correct doses of the antibiotic subconjunctivally. Such levels are slightly higher than those reached with equal doses by systemic administration (Sorsby and Ungar, 1946-48; Andrews, 1947).

The degree of impurity shown by the first preparations of the antibiotic did not permit the quantity of penicillin introduced at each injection to exceed 10,000 to 20,000 units dissolved in 0·5 ml. distilled water. The high degree of purity obtainable at the present time, and the perfect solubility of the substance, now permit the introduction of 500,000 to 1,000,000 units dissolved in 0·5 ml. distilled water, preceded by a simple cocaine anaesthesia. These large doses admit the advantage of reaching the highest concentration in the aqueous and ocular tissues, but do not prevent the rapid elimination of the substance from the subconjunctival area backward through the lymphatic epibulbar spaces. This constitutes a great obstacle to the common use of the drug in subconjunctival injections, on account of the frequency with which the injections must be administered.

Some substances have recently been tested to discover an agent which, when injected locally with penicillin, will to some degree retard its absorption.

In order to determine the degree to which such substances can retard the absorption of penicillin, we have carried out research, under various conditions, into the rhythm with which the drug passes into the aqueous, together with the blood level. In a series of experiments on rabbits, we tested the efficiency of several associations as follows:

(1) Association of adrenalin 1:1,000 with penicillin.
(2) Association of pectine.
(3) Association of procaine.
(4) Association of procaine-pectine.

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We did not consider the use of penicillin in oil or oil-wax, according to Romansky's formula, because of the particular place where the injection was made. Some tests already made with these substances provoked the formation of hard subconjunctival swellings, which were absorbed with great difficulty, and caused considerable reactive symptoms.

Experimental Technique

The subconjunctival injections were all performed by the same technique. The blood and the aqueous were removed by the same methods and kept in the refrigerator until the moment of estimation. For estimating the penicillin levels we employed the standard capillary tube method (Fleming, 1944).

(1) As a preliminary test we first determined the values obtained in the blood and aqueous after a subconjunctival injection of 100,000 units of pure crystalline sodium "G" penicillin, dissolved in 0·5 ml. distilled water. From Table I it appears that the highest level is reached at the first hour, afterwards the level decreases until the sixth hour. The values obtainable in the blood are clearly lower, and decrease with greater rapidity, reaching zero after the end of the fourth hour.

TABLE I.

Effects of Subconjunctival Injection of 100,000 *U. Crystalline Penicillin "G" in* 0·5 *ml.* H_2O.

Penicillin Levels	Test Animals	Number of Hours after Injection							
		1	2	4	6	10	14	20	24
Aqueous (units per ml.)	1	>30	10	2	0·3	0	—	—	—
	2	>20	10	0·5	0	—	—	—	—
	3	16	8	1	0·2	0	—	—	—
Blood (units per ml.)	1	12	4	0	0	—	—	—	—
	2	6	1·5	0	0	—	—	—	—
	3	8	2	0·2	0	—	—	—	—

(2) According to the repeated experiments of Sorsby and Ungar the subconjunctival introduction of adrenalin (1 in 1,000) as solvent of the penicillin raises the levels and prolongs the permanence of the antibiotic both in the aqueous and in the blood. These results, already seen in low doses of the drug (20,000 to 50,000 units), are much better defined, as is shown by the above mentioned authors, through the subconjunctival introduction of 1,000,000 units in the same solvent.

As in the test made without adrenalin, we introduced subconjunctivally 100,000 units of pure crystalline penicillin "G" in 0·5 ml. adrenalin (1 in 1,000). The results are shown in Table II.

From the above table it clearly appears that adrenalin exerts a marked effect in raising the level of penicillin in the aqueous and in causing a longer persistence of the antibiotic. On the blood levels the retarding effect is less pronounced,

but nevertheless quite recognizable; at the sixth hour, and sometimes at the tenth hour, it is possible to find penicillin present in the blood, whereas without adrenalin the blood levels are close to zero after the fourth hour.

(3) Because of some results, rather clinical than experimental, pectine was suggested as a possible agent of retarding the absorption of penicillin, but tests of its efficiency in subconjunctival injections all failed.

TABLE II.

Subconjunctival Injection of 100,000 *U. Penicillin in* 0·5 *ml. Adrenalin Solution* (1 in 1000).

Penicillin Levels	Test Animals	Number of Hours after Injection							
		1	2	4	6	10	14	20	24
Aqueous (units per ml.)	1	>20	>20	>16	4	0·5	0·1	0	—
	2	>30	30	10	2	1	0	—	—
	3	24	>16	16	4	1	0·2	0	—
Blood (units per ml.)	1	6	3	>1	0·2	0	0	—	—
	2	4	2	2	1	0·5	0	—	—
	3	4	4	1	0·5	0	0	—	—

We employed a colloidal solution of pectine 2 per cent. in water adjusted to a *p*H of 7·2; the penicillin was easily dissolved in the same proportion of 100,000 units in 0·5 ml. of the pectine solution.

The values obtained with the titration tests *in vitro* in the aqueous and blood are given in Table III.

TABLE III.

Subconjunctival Injection of 100,000 *U. Penicillin dissolved in* 0·5 *ml. of a* 2 *per cent. Pectine Solution.*

Penicillin Levels	Test Animals	Number of Hours after Injection							
		1	2	4	6	10	14	20	24
Aqueous (units per ml.)	1	>10	6	2	2	0·5	0	—	—
	2	8	4	—	1	0·2	0	—	—
	3	>8	>4	—	0·5	0·2	—	—	—
Blood (units per ml.)	1	4	4	2	0·2	0	—	—	—
	2	4	1	0·5	0	0	—	—	—
	3	6	>2	1	0·2	0	—	—	—

From the results obtained we concluded that pectine does show in reality a certain action in retarding the elimination of penicillin from the subconjunctival areas; but this action seems considerably limited compared with that shown by adrenalin. These results perhaps explain the mechanism through which pectine exerts its retarding action. This action, which is evidently developed *in situ*, must be bound up either with molecular complexes arising locally, or with a reduction in permeability of the local capillaries.

(4) The use of an insoluble salt of penicillin-procaine, either in water or oil suspension, has already been commonly employed in systemic administration. By this means the aim has been achieved of maintaining a therapeutic level of the antibiotic in the blood for a long time. In our experiments we used a preparation of penicillin-procaine in aqueous suspension, in which no foreign substances beyond a small amount of dispersing and stabilizing agents are present. The subconjunctival use of this drug did not provoke any noteworthy disturbance in the rabbit. The only points to be careful of are firstly to avoid the needle penetrating the blood vessels during the injection, secondly, to use a larger needle than that commonly employed in subconjunctival injections in order to prevent the occlusion of the lumen.

TABLE IV.

Subconjunctival Injection of 100,000 *U. Procaine-penicillin "G" suspended in* H_2O.

Penicillin Levels	Test Animals	Number of Hours after Injection							
		1	2	4	6	10	14	20	24
Aqueous (units per ml.)	1	20	>12	8	4	1	0	0	—
	2	16	10	4	2	0·5	0·2	0	—
	3	>16	>10	6	1	1	0·5	0	—
Blood (units per ml.)	1	6	6	4	4	>2	2	0·5	0
	2	>4	4	4	2	1	1	0·5	0
	3	6	>4	—	2	1	0·5	0·2	0

Lower concentrations are present at the first hour compared with those obtained by using penicillin dissolved in distilled water. On the contrary therapeutic levels of penicillin are found in both aqueous and blood as long as 14 hours after the injection. In some tests traces of penicillin were found in the blood up to 20 hours after the injection. Comparing this with the results obtained by the use of penicillin-adrenalin we notice that, while in the aqueous the values appear to be nearly similar, in the blood they seem higher and much more persistent.

(5) Finally we investigated the retarding action on the absorption of penicillin in the same experimental conditions, by a combination of procaine-pectine in colloidal solution. In this case also the combination with penicillin leads to the formation of some insoluble crystals of procaine penicillin. By carrying out the injection promptly we avoided the formation of these crystals, which only appear after 15 to 30 minutes.

From these results it is clear that the association of procaine-pectine affords no advantage in comparison with that obtained by other retarding processes; it is rather inferior to that of procaine alone.

Conclusions

All the different substances having the faculty of retarding the absorption of penicillin by local action which we tested promote some degree of permanence in the subconjunctival spaces, when introduced subconjunctivally with penicillin.

TABLE V.

Subconjunctival Injection of 100,000 *U. of Penicillin in Procaine-pectine Colloidal Solution.*

Penicillin Levels	Test Animals	Number of Hours after Injection							
		1	2	4	6	10	14	20	24
Blood	1	6	6	4	1	1	0	—	—
	2	10	>4	4	2	0·5	0·2	0	—
	3	10	6	2	2	0·5	0·2	0	—
Aqueous	1	4	4	2	1	1	0·5	0	—
	2	4	2	—	1	0·5	0·2	0	—
	3	>2	2	1	—	1	0·3	0	—

The intra-ocular penicillin levels, as can be seen from the values we found in the aqueous, are generally higher and much more persistent.

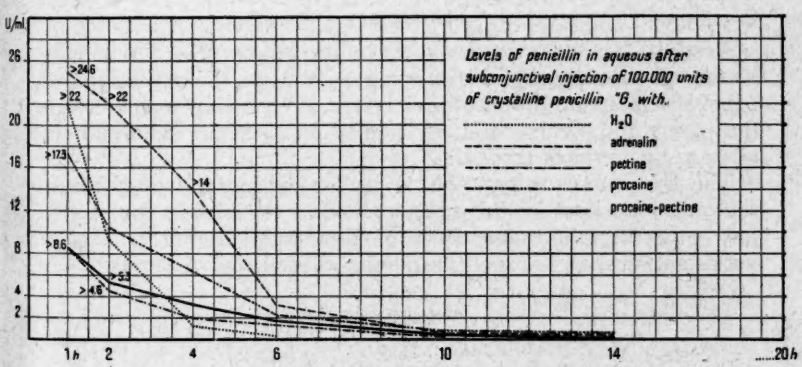

FIG. 1.—Graph showing mean penicillin levels in aqueous calculated from three experiments; details in Table I (H_2O), Table II (adrenalin), Table III (pectine), Table IV (procaine), Table V (procaine-pectine).

The most effective agents seem to be penicillin-procaine and penicillin-adrenalin. The first promotes high intra-ocular peni-

cillin levels and also more persistent concentrations in the blood, which are close to those obtained by parenteral injections of the penicillin-procaine combination, and the second promotes heightened intra-ocular levels. (Figs 1 and 2)

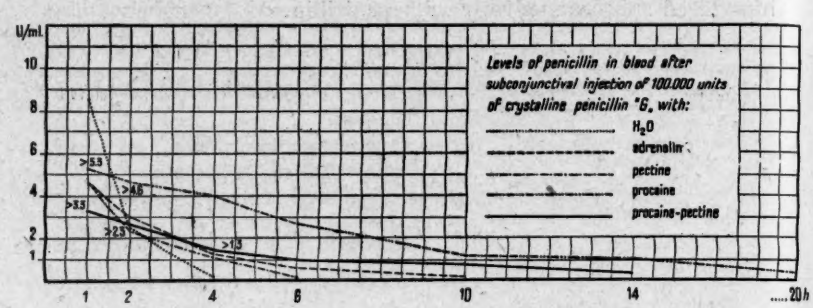

FIG. 2. Graph showing mean penicillin levels in blood calculated from three experiments; details in Table I (H_2O), Table II (adrenalin), Table III (pectine), Table IV (procaine), Table V (procaine-pectine).

From the foregoing considerations it appears that, among the substances which develop a local retarding action, penicillin-procaine and penicillin-adrenalin are of the greatest importance, as being the most active in retarding the absorption of the antibiotic and in giving higher and more prolonged intraocular levels.

Summary

A study has been made of the effectiveness of different substances possessing a local retarding action, on the absorption of penicillin introduced subconjunctivally. According to these tests the penicillin-procaine and the penicillin-adrenalin combinations seem to be the most active.

The first succeeds particularly in prolonging the presence of the antibiotic both in the aqueous and in the blood; the second has only the important effect of promoting higher and more persistent intra-ocular concentrations of penicillin.

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A CASE OF PERMANENT BLINDNESS DUE TO TOXAEMIA OF PREGNANCY*

BY

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THE fact that permanent blindness is such a rare complication in the toxaemia of pregnancy has prompted me to set the following case on record.

I can find no account of permanent blindness resulting from pregnancy in the records of the Rotunda Hospital, Dublin. Certainly no case has occurred in the last 73,572 pregnancies covered by the hospital (1935-48), and three Masters who held office before 1935 (Dr. Fitzgibbon, 1919-26; Dr. Bethel Solomons, 1926-33, and Dr. Davidson, 1932) have kindly allowed me to state that during their periods of mastership no case of permanent blindness occurred. Thus, this case appears to be the first in over 150,000 births. Since the classification of what constitutes "toxaemia of pregnancy" has undergone modification during the last 30 years, it would be valueless to give statistics. Any marked degree of permanent reduction in sight after toxaemia of pregnancy has been an unusual occurrence in the Rotunda Hospital. No mother in these last 73,572 births has required blind assistance as a result of her pregnancy.

An investigation of the literature has produced only one case of permanent blindness due to pregnancy toxaemia. A 30-year-old woman had a transient loss of sight on her third pregnancy, lost the sight of one eye (with marked diminution in the other) on her fourth pregnancy, and went totally and permanently blind on the fourth day after the birth of her fifth child. Six years later she developed presenile dementia. She was examined generally and ophthalmologically seven weeks after the birth of her fourth child, and again two years after going blind following her fifth pregnancy. On both occasions the urine showed no albumen and exhaustive examination of the central nervous system revealed no abnormality. There is no record of urine analysis or blood pressure. Her blindness was caused by post-neuritic atrophy.

Case Report

History.—The patient, 26 years of age, was admitted (January, 1949) to the Rotunda Hospital in the 35th week of her sixth pregnancy. Her four previous pregnancies had been normal full-term deliveries. In none had she suffered from

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toxaemia, or had any visual symptoms, or transient loss of sight. She had never had any serious illnesses (measles in childhood, appendicectomy two years previously). Her only complaint was intermittent headaches for some years.

General Condition.—She was admitted as an emergency with the diagnosis of "pre-eclampsia". Her general condition was described as "fairly good". She was conscious and rational. There was no generalized oedema. Blood pressure was 220/170; urine showed "albumen abundant"; temperature 98°; pulse 106. At no time before or after delivery did she have convulsions. Caesarean section was carried out the day after admission, and a live male baby of 4½ lbs. was delivered. The baby was healthy, and has continued to thrive. After operation the patient developed paralytic ileus and became acutely ill. She remained in hospital for over three months, and on discharge was reasonably well. The diagnosis was toxaemia of pregnancy.

Ophthalmic Condition.—The patient stated that two weeks prior to admission her sight had become blurred, and that for the last two days it had begun to fail rapidly. No previous loss of sight had occurred during pregnancy.

On admission the right pupil was inactive to light; the left was active. Vision in the right eye was reduced to no perception of light and in the left to counting fingers at a distance of one foot. Both fundi showed marked oedema of the disks and surrounding retina with haemorrhages and cotton wool exudates. There was severe generalized angiospasm. The retina in the lower part of each fundus was detached, shallow in the lower nasal quadrant but deep and globular in the lower temporal quadrants. Eight days later the detachments were a good deal less, the retinopathy was unchanged, but vision was now reduced in both eyes to no perception of light.

Three weeks after admission the ocular condition was:

R.E., disk and surrounding area of retina less oedematous. Vessels still very small. Fewer haemorrhages and exudates. Detachment small, 5 to 8 o'clock only. Pupil dilated and inactive to light, active with convergence. Vision, no perception of light.

L.E., very little blurring of disk margin. Disk paler than R. Fewer haemorrhages and exudates. Scattered pigmentation appearing in fundus at site of old haemorrhages and exudates. Detachments much smaller, confined only to the lower and outer quadrant. Vessels still very small. Pupil widely dilated and inactive to light, active with convergence. Vision, no perception of light.

On discharge the condition was: fixed mydriasis. No retinal detachment. Both optic disks showed an advanced degree of secondary atrophy with gross constriction of vessels. The retinal arteries were scarcely visible. There was no perception of light in either eye.

Diagnosis.—A diagnosis of bilateral total transverse neuritis can be made with certainty in this case. The neuritis had occurred near the nerve head, thereby producing papilloedema and, as is usual in such cases, resulting in secondary atrophy.

Discussion

The interest from the purely ophthalmological view-point lies in the aetiology of this rare condition. In an attempt to determine this the patient was admitted twelve months later (January, 1950) to the Royal City of Dublin Hospital, where Prof. Synge undertook a complete investigation.

The following tests were carried out: Urine analysis; blood pressure; uroselectan; cystogram; *X* ray of sinus and pituitary; and full investigation of the central nervous system. Apart from the blood pressure and urine analysis nothing abnormal was found. The blood pressure varied between 225/170 and 235/170. The urine contained albumen, pus, and an occasional hyaline cast. Blood urea was 25 mg. per cent. The Ascheim-Zondek test for pregnancy was positive, and it was considered

that she was some two months pregnant. Ophthalmological examination showed bilateral fixed mydriasis, advanced secondary optic atrophy, and severe generalized angiospasm with gross notching of the arteriovenous crossings. Vision in the right eye was no perception of light, but in the left there was a definite occasional light perception in a small area downward and outward.

The toxin, if toxin it be, of pregnancy toxaemia remains unknown. It must be recollected too, that the existence of a toxin is challenged by many investigators. Thus Falkiner (1950), following his work on the placenta, considers the condition to be "secondary to vascular disturbances consequent on arteriolar spasm." In a routine series of 204 toxaemia cases that I have investigated in the Rotunda Hospital, 43·6 per cent. showed either localized or generalized angiospasm of the retinal arteries, Pickering (1950) on the other hand has never seen spasm of the retinal arteries in pregnancy toxaemia. The view of Bastiaanse (1950) is that the toxaemia is related to an absolute or relative insufficiency of the blood supply to the placenta. All are agreed that the fundamental clinical finding in toxaemia is high blood pressure, and that the kidney dysfunction is secondary. Retrobulbar neuritis producing transient loss of sight, often very dramatic but unassociated with fundus changes, is relatively common. Full vision normally returns.

We know that total occlusion of the central retinal artery (whether by spasm or embolism) produces sudden and deep blindness; and also that if the occlusion persists long enough, the blindness becomes permanent. These arterial blocks usually take place in the region of the cribriform plate, and may therefore be considered as too far forward in the nerve to produce papilloedema. The case under review exhibits extreme generalized angiospasm of the ophthalmoscopically visible retinal arteries, It is suggested that the papilloedema which was present in this case could follow a severe spasm of the entire retinal artery. The spasm by its persistence, would result in blindness and secondary optic atrophy. There is a possibility that oedema of the brain by producing increased intracranial pressure could account for the bilateral papilloedema that I have observed in severe toxaemia cases, always associated with eclampsia, gross generalized oedema, and retinal detachments. The papilloedema clears with the subsidence of the general oedema and improvement of the condition. Angiospasm would also explain the transient loss of vision in pregnancy toxaemia. Indeed it is difficult to account for the transient haemianopia which is by no means a rare concomitant of toxaemia, by any other hypothesis. Angiospasm as a cause of optic atrophy would also fall in well with the findings of Mooney and

McConnell (1949). These investigators consider that the optic atrophy found in space-occupying lesions in the region of the carotid tree results, not from direct pressure on the nerve or chiasma, but from interference with their blood supply.

Conclusion

This therefore must be considered a case in which total transverse neuritis resulted as a concomitant to toxaemia of pregnancy in an otherwise healthy woman. The unusual general features were the absence of convulsions or severe oedema and the fact that neither transient blindness nor toxaemia had occurred in previous pregnancies.

It is suggested that the retrobulbar neuritis in this case is the result of angiospasm, and that angiospasm also plays a dominant rôle in other ocular conditions resulting from the toxaemia of pregnancy.

My thanks are due to Dr. O'Donel Browne, Master of the Rotunda Hospital, who kindly permitted me to publish this case, to Dr. Ninian Falkiner, late Master of the Rotunda Hospital, who added his advice on this case to much already given, to the three previous Masters, Dr. Gibbon FitzGibbon, Dr. Bethel Solomons and Dr. Andrew Davidson, who all gave me assistance and advice, and to Dr. Desmond Douglas who made the first records of this case and has subsequently followed it up with me.

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THE INDICATIONS AND TECHNIQUE OF IRIDENCLEISIS*

BY

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FEW surgical techniques have provoked as many *a priori* objections as iridencleisis. The numerous cases of raised tension and iritis, often attended by the danger of sympathetic ophthalmia, observed after accidental or post-operative iris inclusions, contra-indicate any operation in which a tag of iris tissue is left under the conjunctiva in direct communication with the anterior chamber. It seems, however, not only that iridencleisis is no more dangerous than other fistulizing operations (Lagrange, 1922; Elliot, 1913), but also that this operation is suitable for many serious cases of chronic glaucoma, and in subacute glaucoma, and in glaucoma secondary to iritis, where any other fistulizing device may be dangerous.

Having analyzed for the International Congress of 1950 my personal statistics of more than 1,100 cases of fistulizing operations, I have been able to establish that in 236 cases of iridencleisis for chronic glaucoma, the percentage of successes was higher than that achieved by any other technique (Lagrange, 1922; Holth, 1930; Elliot, 1913). Moreover, a more detailed study has enabled me to confirm that the operation had usually been undertaken under the most difficult circumstances (with a restricted peripheral field or considerably reduced central vision), and also that it had been successfully used in cases of subacute glaucoma or hypertensive iritis. It seemed to me, furthermore, that my views on the indications and technique of this procedure might help to clarify the disputed question of its value.

Surgical Indications

Chronic Glaucoma.—The majority of our iridencleises were done in cases of chronic glaucoma, "wide-angle glaucoma", if we accept the classification adopted at the Chicago Symposium on primary glaucoma (1948), despite the pertinent and detailed criticism offered, particularly by Duke-Elder (1949). With variations, largely due, no doubt, to their greater or lesser natural aptitude for surgery, the oculists of different countries to-day seem to admit that in this type of glaucoma the surgical era has not come to an end, and that the

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operation is necessary when medical treatment is non-effective or has ceased to be of value. Basing my opinion on the analysis of the 1,100 cases mentioned above, I think that " wide-angle glaucoma " should be operated upon without delay, if medical treatment fails to control the condition. In settling the right time for operation, the central visual acuity, visual fields, and ocular tension must be considered together. In the light of my own experience I hesitate to operate while the vision is above 8/10, unless the peripheral field is contracting rapidly. The paracentral scotomata seem to be less significant as a pointer for operation, because they do not always yield to the normalization of pressure. The interpretation of tonometric curves also seems worthy of comment. The actual level of the pressure is not decisive. Many of our patients with relatively low pressures—from 32 to 35 mm. Hg—had already suffered marked shrinkage of the visual fields as well as reduced central acuity. Others, despite pressures between 40 and 45 mm. Hg, maintained satisfactory central and peripheral acuity. In the important papers read at the Chicago Symposium I have found no mention of the relation between tonometric figures and those provided by the study of systemic and retinal arterial pressures. Bailliart's pupils, however, have all for a long time been taught the importance of that relation, and the eldest of them feels it his duty to emphasize the relatively benign effect of retinal and general arterial hypertension on ocular hypertonicity. I have seen examples of a rapid fall in central visual acuity and of a sudden contraction of the visual field after a cardiologist, with little ophthalmological training, had drastically lowered the arterial pressure. In the same way one must stress the psychological and environmental conditions in which tonometric measurements must be made. Emotion in a glaucomatous patient (vago-sympathetic imbalance) can alter the pressure. Likewise undue mobility of the globe, and lid-spasm, can influence the tonometer reading. Tonometric figures—like those of any over-precise test—must be interpreted with discrimination.

Certain associated features hasten the need for operation in glaucoma. Hereditary glaucoma is particularly serious. Psychologically, the fear of blindness in patients whose relatives have been so afflicted may be a contributory factor, although the actual state of the eye often decides the issue. One last factor—not of a scientific nature—may also necessitate early operation. A patient leading a busy life, or one who lives far out in the country, is often more difficult to keep under observation, and in such cases the insidious advance of glaucoma may render early operation imperative.

These conditions are indeed common to all operative procedures

designed to combat chronic glaucoma. *A priori* fears of iridencleisis deterred me for a long time from using it except in the most unfavourable cases, with very contracted peripheral fields and greatly reduced central acuity. Since the results have been relatively successful, as the following Table indicates, I have

TABLE

Iridencleisis in Chronic Glaucoma

Analysis of Material			Numbers		Percentages	
Total Cases of Chronic Glaucoma			615		—	
Iridencleisis performed	as a single operation		225	236	—	
	after another fistulizing operation ...		11			
Results ...	successes (ocular pressure reduced) ...		221	236	93·6	100
	failures (ocular pressure remained high and operations followed by ocular atrophy or enucleation)		15		6·4	
Visual Acuity	before operation	L.P. or H.M. ...	55	236	23·3	100
		below 3/10	72		30·5	
		3/10—5/10	44		18·6	
		5 5/10—8/10	33		14·0	
		above 8/10 (field severely reduced)	32		13·6	
	after operation	improved	105	236	44·5	100
		no change	94		39·8	
		lowered	37		15·7	

increasingly used the technique in less serious cases. Even to-day, however, I use it as a last resort in the worst cases of chronic glaucoma; when both eyes must be operated on and a different technique is employed for each, iridencleisis is performed on the more seriously affected eye.

Subacute Glaucoma.—In this type (which has been termed inflammatory glaucoma, and is often classed as a " narrow angle

glaucoma") iridencleisis seems to me again to be clearly indicated. The problem here is not merely one of opening the filtration angle, as in acute glaucoma, but also of ensuring permanent fistulization. It is known that simple iridectomy, which is usually sufficient to deal with acute exacerbations of hypertension, is inadequate in combating the residue of chronic hypertension which distinguishes this type of glaucoma from the true acute variety. It is well-known, moreover, that sclerectoiridectomy performed in an acute phase usually ends in obstruction. For a long time it has been my practice to perform a preliminary iridectomy in an oblique meridian (at 2 or 10 o'clock) and then, when the eye is quiet again, to carry out a fistulizing operation on the other side of the vertical meridian. It seems to me that iridencleisis, even when performed in an acute phase, is usually adequate to overcome simultaneously the phenomena of chronic hypertension, and I now use it regularly in treating such cases.

Hypertensive Uveitis.—Marcel Kalt, in his excellent report presented in 1949 to the Société française d'Ophtalmologie, follows Weekers (1947) in advising the use of iridencleisis in hypertensive uveitis, and I support him in this opinion. One reservation must, however, be made. Uveitis with hypertension occurs in two essentially different types of case. In some cases, the hypertension is an integral element of the syndrome and is present from the onset, as if vago-sympathetic imbalance and oedema of the vitreous were essential characteristics of the uveal disturbance. In other cases, the hypertensive phenomena, developing later, are secondary to pupillary occlusion. This is the situation in certain cases of syphilitic and of fibrinous iritis. In this second type of case, iridectomy, less traumatizing even than iridencleisis, is sufficient, provided that it be performed in time, since there comes a time when it can no longer be risked. It would be correct to say that iridectomy must prevent rather than treat seclusion or occlusion of the pupil.

Chronic glaucoma, subacute glaucoma, hypertensive iritis—these are the major indications for iridencleisis. The severity of these conditions, however, necessitates a rigorous surgical technique upon which I feel bound to insist.

Technique

In my belief, iridencleisis, the value of which is great but more or less comparable with that of other fistulizing operations in the early stages of chronic simple glaucoma, is the best operation for chronic glaucoma of long standing, in which there is a marked

reduction of central vision and a large degree of contraction of the visual field. It has been shown that it should also be used in cases of subacute glaucoma and of hypertensive iritis. For this reason it must be performed with great care, operative trauma being reduced to a minimum and haemorrhage avoided at all costs; the latter may arise from dilatation of blood vessels or from rapid decompression.

Induction of anaesthesia may be difficult with red eyes, which often require operation. Adrenalin, ephedrine, and privine should be instilled for a prolonged period. The retrobulbar injection should consist of equal parts of 4 per cent. procaine and of ephedrine, with a few drops of adrenaline.

I usually increase the coagulability of the blood by giving two injections of " coagulène " (platelets and thrombin) and three injections of " adrénoxyl " (monosemicarbazone of adrenochrome, 0·05; sodium chloride, 0·010; acid sodium and potassium phosphate, 0·058; potassium dihydrogen phosphate, 0·035; distilled sterile water, to 100 ml.).

The eyeball is firmly fixed by a stitch placed in the superior rectus, and the bulbar conjunctiva is dissected with scissors and then with a Desmarre scarifier, dissection being carried to the limbus as in any other fistulizing operation. Haemorrhage from the scleral vessels is controlled by application of the point of a strabismus hook at dull red heat. I almost always use the *incisio ab externo* of Gayet, with a thin-bladed knife (razor blade). The linear incision, 4 mm. long, is made tangentially to the limbus and 1·5 mm. above it, at the level of the root of the iris. It is performed very carefully like a cyclodialysis incision, but here bulging of the root of the iris serves as a warning that the sclera has been pierced. When the prolapsed iris root is the size of a pin-head, the operation is stopped for 30 or 40 seconds to allow the gradual escape of aqueous; this procedure appears to be extremely important.

If the atrophy of the iris is too great or there are dense adhesions to the lens capsule, spontaneous prolapse of the iris may not occur. When the aqueous has been slowly evacuated, slight pressure on the cornea often causes prolapse of the iris root into the wound, with negligible trauma. I should add that advanced iris atrophy is of bad prognostic significance, and in these cases the technique of operation should be modified. I shall refer to this again later in the paper.

When the scleral incision has been completed, the iris usually protrudes in spite of the loss of aqueous. It is then retained by a rather special method, similar to that described by Pillat (Meller and Böck, 1946). The aim is to avoid return of

the iris into the anterior chamber. This is easily achieved by dividing the sphincter, without touching the base of the iris, which should be allowed to form a lip over the scleral wound, thus preventing its closure. I prefer this technique to the dilaceration recommended by Weekers—a dilaceration which, in my view, is more likely to lead to haemorrhage than the clean section used by Pillat and myself. The difference between Pillat's technique and mine is slight—I section the iris from bottom to top, from the pupillary margin towards the lesser circle. The conjunctival flap is replaced with a continuous silk suture without knots at the ends. Except in cases of subacute glaucoma, I usually instil a drop of atropine at the end of the operation.

Haemorrhage is usually slight if the precautions described above are observed: increase of coagulability of the blood by drugs, careful haemostasis of scleral vessels, slow release of the aqueous, and clean sectioning of the iris sphincter. I have sometimes used diathermy for the last step when, under the slit-lamp microscope, the vessels of the iris appeared excessively dilated.

Advanced iris atrophy seems to me to endanger filtration. In these cases I modify my technique. After turning back the conjunctival flap, I make a second incision parallel with and 1·5 mm. below the first incision, and dissect up a thin band of sclera. I then cut the iris right to its base, and wedge the free margins into the angles of the resected zone. This relatively simple modification has often permitted good results to be obtained in cases in which iridencleisis performed by my usual technique would have seemed doomed to failure.

I do not wish to refer again to the detailed statistical analysis of my cases of iridencleisis. For the statistics to be of value, the conditions in which the method was practised must be studied. In brief, it can be said that, out of 236 cases of iridencleisis for chronic glaucoma in which the results could be checked, there were fifteen failures (6·4 per cent.). In 85·3 per cent. of cases we were able to maintain or improve visual acuity, visual field, and ocular pressure. In almost all of these cases, there was permanent filtration, so closely comparable with the filtration obtained by Lagrange's operation that we could not always tell which technique had been used without consulting the case history. In eight cases I had to perform an enucleation in order to prevent the development of sympathetic ophthalmia, a complication which I have never encountered.

The results of the use of iridencleisis in hypertensive iritis are certainly less favourable. In subacute glaucoma, on the other hand, they are at least not inferior to those obtained in the treatment of chronic glaucoma.

Until fuller knowledge of the causes and mechanisms of the different types of ocular hypertension allows us to obtain equally good results with medical treatment alone, I am convinced of the injustice of many of the criticisms raised against the surgical treatment of the disease. Techniques improve, and must continue to do so, but the idea, which Lagrange had the good fortune to put into practice first, of permanent drainage of the aqueous into the sub-conjunctival space has already enabled a large number of patients to conserve their vision. Iridencleisis seems to me to permit the extension of these results to cases in which other techniques of fistulization would be ineffective.

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A NOTE ON THE SO-CALLED ENLARGEMENT OF THE BLIND SPOT IN GLAUCOMA*

BY

P. L. BLAXTER

London

ABOUT sixty years ago Bjerrum described his method of investigating the central fields in cases of glaucoma, and after the publication of Seidel's findings (1915), it became the custom to describe the central field changes in glaucoma as wedge-shaped scotoma arising from the blind spot, and progressing to form Bjerrum's arcuate scotoma, which process was frequently described as "enlargement of the blind spot". This was the universally accepted state of affairs until the late nineteen twenties, although one does find the occasional reference to the occurrence of scotoma arising away from the blind spot (van der Hoeve, 1915; Elliot, 1921). However, Traquair (1931) pointed out that even if the arcuate scotoma did develop in this way, the term "enlargement of the blind spot" was not justified as it was more applicable to the condition found in cases of papilloedema, or coloboma of the optic disk. He further showed that when working with small test-objects, the earliest defects were found to be scotoma arising away from the blind spot and only joining it later to form the arcuate scotoma, and this opinion he has maintained in later publications.

It is therefore somewhat confusing to find that recently published textbooks still adhere to the original description of the development of the Bjerrum scotoma and use the term "enlargement of the blind spot". In view of this diversity of opinion, it was felt to be of interest to try to establish the site of origin of the arcuate scotoma by investigating the central fields of patients whose clinical histories suggested the possibility of early glaucomatous changes.

Thirty-five such cases were investigated on the Bjerrum screen at 2 metres. All fields were done with white objects from 20 mm. to 2 mm. (The 1 mm. object was not satisfactory on this screen as it was frequently not seen beyond the 15° circle by normal subjects.) Of the cases examined fifteen were found with scotoma only demonstrable with small objects and therefore presumed to be early defects. It appears from these cases that, apart from baring of the blind spot to a 2 mm. object, the earliest defect is a

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scotoma only demonstrable with small objects which appears in the temporal field, most frequently the upper, from 15° to 25° from the fixation point, and not connected with the blind spot. This scotoma later enlarges and runs into the blind spot, but it is then usually possible to locate a more dense nucleus not yet connected with it. In one case a scotoma with no nucleus was found connected to the blind spot. This scotoma was not wedge-shaped, and was narrowest at its junction with the blind spot.

In no case was the blind spot found to be enlarged, and it seems that this term is not applicable to the perimetric changes in glaucoma.

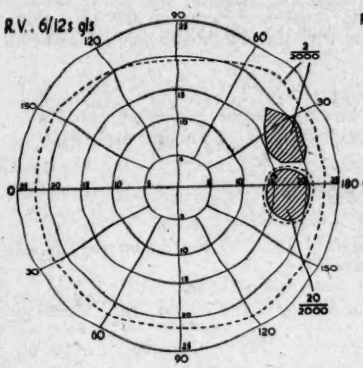

FIG. 1.—Case 1, F.R., male, aged 51.

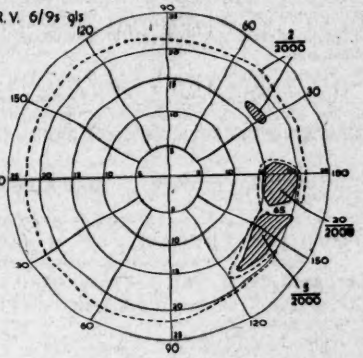

FIG. 2.—Case 2, P.N., male, aged 44.

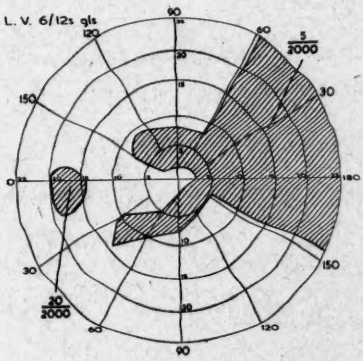

FIG. 3.—Case 3, M.D., female, aged 56.

Case Histories

The following cases are selected to illustrate these points:

Case 1. F. R., male aged 51 (Fig. 1). Recurrent attacks of haloes and misty vision in R.E. since 1947. No abnormality found until December, 1949, when he appeared one evening with a typical attack of sub-acute glaucoma which settled with eserine. Optic disks normal. Peripheral fields full. R. central field shows a typical early scotoma. L. central field full. Admitted for R. trephine.

Case 2. P. N., male aged 44 (Fig. 2). Bilateral trephine January, 1948. Condition has remained stationary since. R. peripheral field normal. L. shows gross constriction. R. central field shows baring of the blind spot with a small scotoma above it and a more dense one below.

Case 3. M. D., female aged 56 (Fig. 3). September, 1949, cupping of left optic disk, noticed on routine examination. No symptoms. L. trephine October, 1949. R. peripheral field full. Central field shows baring of blind spot (2 mm. object). L. peripheral field shows nasal constriction. Central field shows arcuate scotoma above and below the fixation point, breaking through on the nasal side. (This is an example of a fairly advanced case with the defects still well clear of the blind spot.)

My thanks are due to Mr. Eugene Wolff for the advice and encouragement he has given me, and to the surgeons of the Westminster branch of Moorfields, Westminster and Central Eye Hospital for permission to publish these cases.

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A SIMPLE METHOD OF INSERTING AMNIOTIC MEMBRANE GRAFTS INTO THE CONJUNCTIVAL SAC*

BY

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THE treatment of chemical burns of the conjunctiva with amniotic membrane is now widely used. A simple and quick method of insertion saves a patient with an already acutely tender eye much discomfort.

An amniotic membrane graft is required to separate two raw surfaces of conjunctiva and prevent the formation of symblepharon. A method is, therefore, needed to hold the graft well into the affected fornix. With this in view Mr. A. J. Cameron suggested inserting a graft into the inferior fornix by means of one double-armed suture, passed through the edge of the graft into the extreme limit of the inferior fornix and out through the skin of the cheek. From this suggestion has been evolved the following technique, which has been found satisfactory in over thirty cases.

Technique

(1) The eye is cocainized with 4 per cent. cocaine drops.

(2) Two small injections of 5 per cent. procaine are given into the skin overlying the affected fornix. (Fig. 2, A and B.) This has been found of value as the patient is less apprehensive of a prick on the skin of the face at this stage than later when he knows that something is being done to his already painful eye.

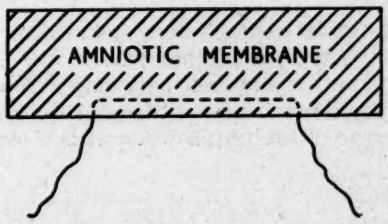

FIG. 1.—Folded membrane with double-armed suture in position.

(3) The amniotic membrane is folded into a shape that will comfortably fit into the fornix and at the same time cover the damaged area of conjunctiva.

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(4) A double-armed suture is then passed through one edge of the graft as shown in Fig. 1.

(5) If the graft is to be inserted into the lower fornix it is first laid on a sterile towel on the forehead. The lower lid is pulled down with the thumb of the left hand, and one needle is passed through the extreme angle of the lower fornix and out through the skin This procedure is then (Fig. 2, A.) repeated, the second needle being brought out at the point B (Fig. 2).

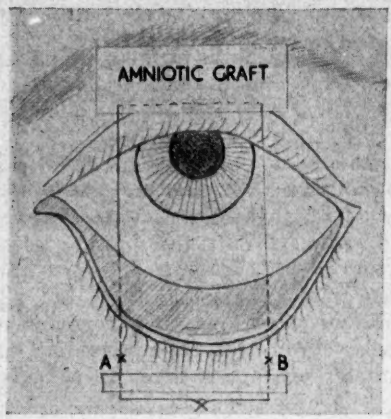

FIG. 2.

(6) The needles are then passed through a piece of rubber tubing of appropriate length and tied, thus drawing the graft well down into the fornix. If the graft tends to wrinkle it is smoothed into position with a squint hook.

(7) Finally an upper-lid suture is inserted to close the eye over the graft and is kept in position for 48 hours by strapping applied to the cheek.

This method can be appropriately modified to place a graft in the upper fornix or to any other part of the conjunctiva that requires protection. It requires only one suture which can be inserted quickly and painlessly, at the same time holding the graft well into the angle of the fornix where it is most needed.

COLOUR PHOTOGRAPHY OF VISUAL PURPLE SOLUTIONS*

BY

H. J. A. DARTNALL

From the Vision Research Unit, Medical Research Council, Institute of Ophthalmology

FOR a recent spectrographic investigation of the light-sensitive retinal pigment visual purple, the results of which will be published elsewhere, it was necessary to prepare solutions of visual purple on a larger scale than has been attempted previously. Generally, about 100 dark-adapted frogs (*rana temporaria*) were used to prepare 50 to 70 ml. of solution. The extraction procedures

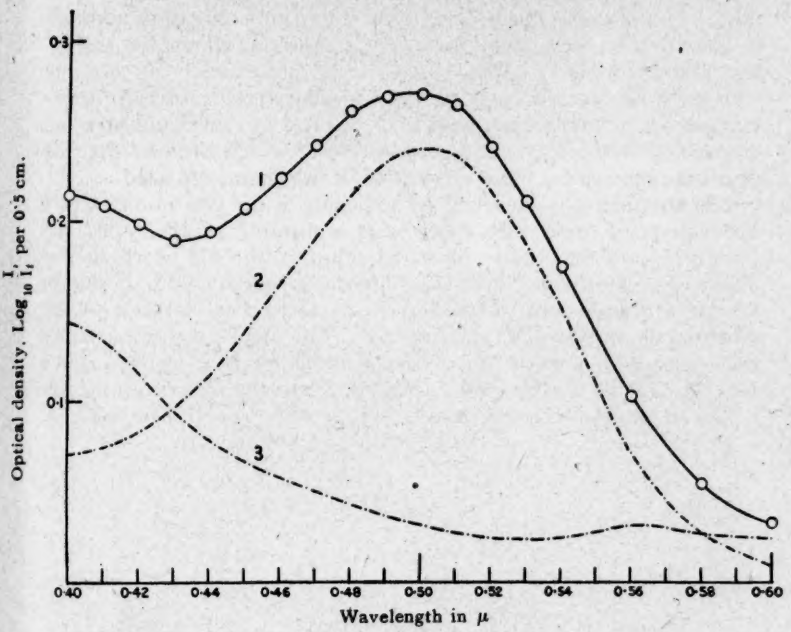

FIGURE.—Curve 1, the absorption spectrum of the unbleached solution; curve 2, the absorption of the contained visual purple; curve 3, the residual absorption due to impurities.

were conducted partly in dim red light and, where possible, in darkness.

The opportunity was taken of obtaining colour photographs of

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an unbleached and bleached solution. The photographs were taken by Mr. S. E. Veronique using Dufaycolor cut film and, as illuminant, a Phillip's P.F.56 flash-bulb in conjunction with the appropriate D2/5 gelatine filter. The conditions for obtaining correct colour values were ascertained by preliminary photography of a similar flask containing a dilute potassium permanganate solution.

Plate I shows the appearance of the solution immediately after withdrawal of the flask from its light-tight container. The solution, which is nearly free from opalescence and slightly frothy due to the presence of the surface active digitonin used as extractive, is reddish and not purple in colour. This is partly due to the presence of yellow substances which are extracted together with the visual purple by the digitonin. The effect of absorption by these impurities may be gauged from the Figure which, in addition to showing the total absorption of the solution, shows the respective contributions of visual purple and impurities. No attempt was made to remove these impurities since these crude digitonin extracts are regarded as preferable material for spectrum analysis to purified solutions, in the preparation of which there is the risk of contamination by trace impurities in the chemicals used.

The solution was bleached by exposing it for two minutes to a 100-watt pearl lamp with reflector at a distance of 18 inches. A photograph of the freshly bleached solution, the *p*H of which was about 6, is shown in Plate II. The deep yellow colour is due to transient orange and indicator yellow, formed as a result of the photodecomposition of visual purple. The modifying influence of the constant absorption of the yellow impurities is, of course, much less marked in the bleached solution, since the absorption of the bleached products is very intense in the same spectral region.

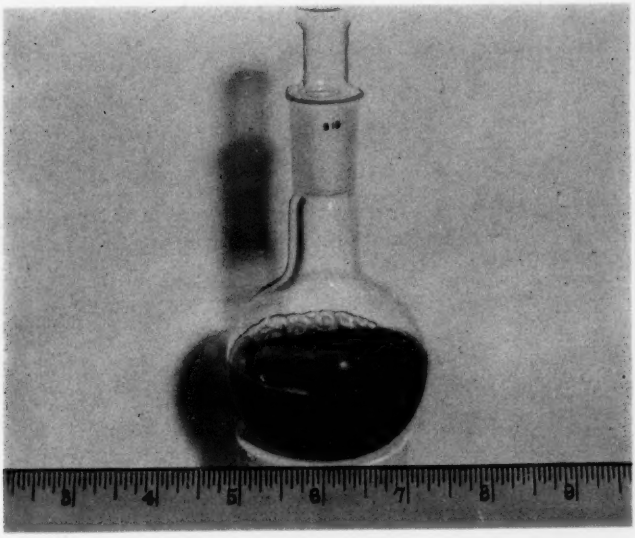


PLATE I

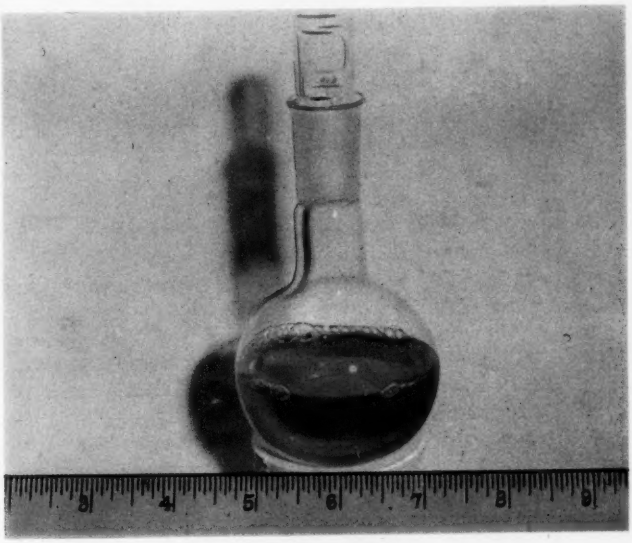


PLATE II

APPLIANCES

A HEAD-CLAMP FOR ORBITAL OPERATIONS*

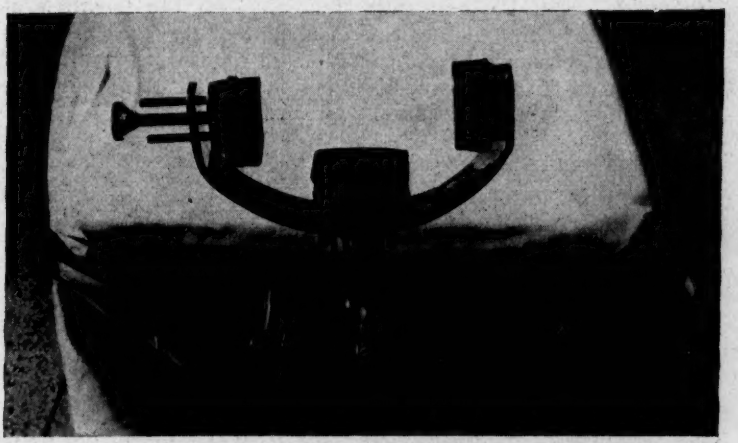
BY

H. B. STALLARD

London

THE advantages of a head-clamp for orbital operations are :

(1) the security of the head against movements when using bone-cutting instruments,
(2) the maintenance of the head at the appropriate inclination and rotation,
(3) improved all-round accessibilty to the field of operation for the surgeon and his assistants.



FIGURE

The Figure shows a head-clamp meeting these requirements which was made for me by Down Bros. It is mounted on a frame secured by screw-clamps to each corner of the head of the operating table. The patient's head rests within an arc, the occiput and temporal fossae make contact with thick sorbo-sponge pads. A screw-clamp secures the head within this arc. The arc is attached to the frame and may be rotated by the screw with its shaft placed obliquely. By turning this screw the arc holding the head may be conveniently rotated so as to incline the head to one side or the other. Such a manoeuvre is of value in lateral orbitotomy (Krönlein's operation), and in dacryocystorhinostomy. Slight elevation of the head is helpful in reducing the amount of oozing during anaesthesia.

* Received for publication March 10, 1950.

The projection of the head-clamp from the end of the table gives the surgeon and his assistant close access without obstruction.

A PLASTIC DISK FOR RETENTION OF A CORNEAL GRAFT*

BY

H. B. STALLARD

London

THE figure shows a transparent plastic disk shaped to the curvature of the cornea, 7 mm. in diameter with four flanges notched on either side about 1·5 mm. from their end, for the retention of sutures passed through the superficial half of the cornea. This disk affords reasonably secure fixation for a corneal graft and at the same time its transparency allows inspection of its edges at the operation and of its position afterwards.

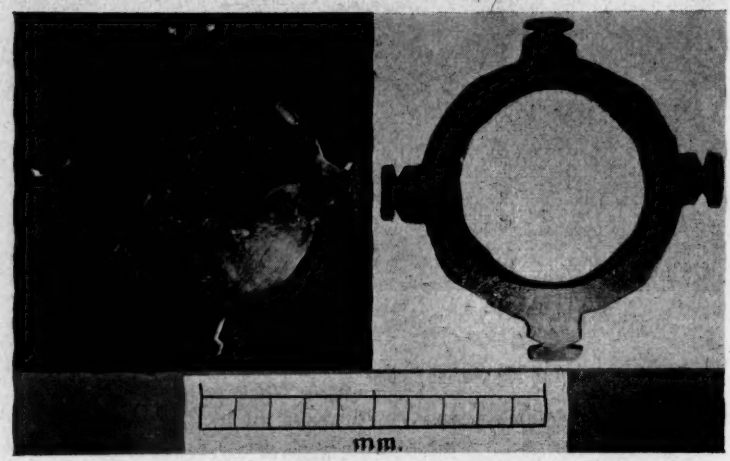


FIGURE.—On the left is a plastic disk. 7 mm. diam., with four notched flanges. On the right is Pittar's tantalum ring for making the site of the graft. The trephine is placed inside the ring which it fits exactly.

The two disadvantages of Pittar's tantalum ring are that it prevents a view of the edge of the graft at the end of operation and afterwards, and that in this ring the centre of the graft is liable to become oedematous and to be compressed forwards in the hole.

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MUSEUM MOUNTING IN OPHTHALMOLOGY*

BY

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THE introduction of transparent plastic materials has stimulated a new interest in the techniques of museum mounting and there are few departments of pathology which have not already abandoned glass museum jars for those composed of Perspex. At the Institute of Ophthalmology the valuable collection of specimens which has resulted from the merging of the museums of the Moorfields, Westminster and Central Eye hospitals, is now being re-catalogued and re-mounted in transparent plastic containers. The purpose of this paper is to give an account of the techniques used, which are based upon the methods employed by other workers, in order that those interested in mounting museum specimens of the eye may have ready access to the various methods available. The majority of the specimens are being re-mounted in a fluid medium in Perspex containers, but solid media such as "Marco S.B. 26C" Resin and Perspex have been used in selected cases, and the results and techniques employed are set out in detail below.

Transparent Perspex Boxes.†—Perspex boxes of length 2¼ in., width 2 in., depth 1 in., and thickness ⅛ in. (Fig. 1) are carefully cleaned, and the back plate, which is sealed in position after the mounted specimen has been placed in the container, is similarly prepared.

A number-plate of opal Perspex is stencilled in indian ink, allowed to dry at room temperature, and then given a coating of Perspex cement on the stencilled side only; it is then inserted so that, when held in position by a single Perspex block internally, the museum number is clearly visible at the lower end of the front of the box (Fig. 5).

Thread holes are now drilled with a twist drill through the thinner centre plate (1/16 in.) and the specimen is firmly tied into position with superfine Nylon sutures (Fig. 3). According to the size of the specimen small Perspex blocks are cut, trimmed, and polished, and fixed in position with Perspex cement. The plate upon which the specimen is mounted is thus held in position by four blocks: lower and upper pairs (Fig. 2).

A hole is drilled in the right hand corner of the bottom of the box through which the container is subsequently filled.

At this stage a circular Perspex plug is prepared by using a fine flat file to reduce a piece of Perspex of convenient length and cross-sectional area of ¼ in. to a smooth rod. The plug should be sufficiently tight to permit of limited but smooth rotation within the fitting hole.

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†These boxes may be obtained ready-made from the "Visijar" Laboratory Supply Co., Ltd., 149, London Road, Croydon, Surrey.

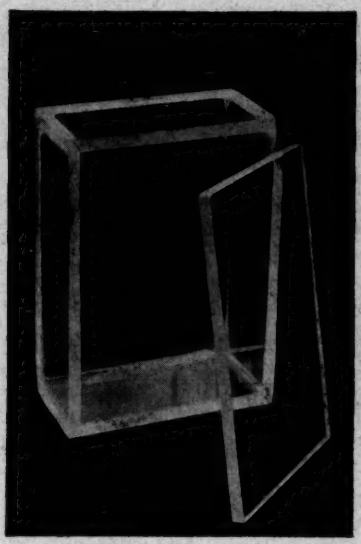

FIG. 1.—Perspex box ready for use. The back-plate is later sealed in position.

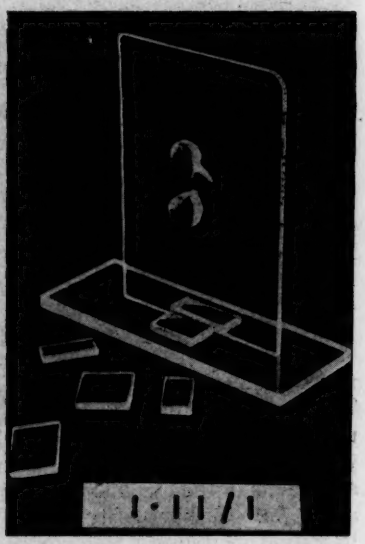

FIG. 2.—The plate upon which the specimen is mounted is held in position by four blocks: lower and upper pairs.

FIG. 3.—The specimen is mounted on the centre plate and tied into position with superfine Nylon sutures.

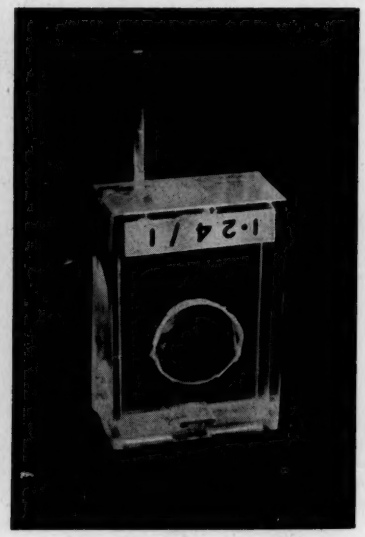

FIG. 4.—The box is filled through a hole in the bottom plate, which is later sealed with a Perspex plug.

The back plate is fixed by clamping after softening the open edges of the box by immersion in chloroform and, when it is completely dry, the mounting fluid is slowly run in. The requisite amount of formalin is now added and finally the sodium hydrosulphite, in amount equivalent to 1 per cent. of the total solution: the crystalline solid being dissolved in a little air-free mounting fluid. The box should be gently rocked to ensure an even diffusion of the hydrosulphite. With this method the natural colours are usually restored within a few days although it may take several weeks for the colour to return completely. Where sodium hydrosulphite is used to restore the colour, Zenker's solution must not be used for fixation; otherwise the specimen will become discoloured by a black deposit.

Sealing is carried out by the following method: the last bubble is positioned below the filling hole by tilting and it is evicted by positive pressure upon the lateral and posterior surfaces of the box. After allowing the box to stand at room temperature for 24 hours, any further bubbles are removed before sealing, which is effected by means of the circular plug previously prepared. The fluid level is adjusted until it is half-way up the filling hole; a large drop of Perspex cement is placed over the hole so that the aperture is covered; the plug, moistened in chloroform and rubbed gently between the finger and thumb until an adhesive surface forms, is then plunged firmly into position (Fig. 4). The plug is left to set *in situ* overnight and when dry is sawn off in close proximity to the surface of the box.

The whole box now receives its final trim. All joins are uniformly rounded with the fine file; they are rendered invisible when the box is (a) coarsely polished with metal polish and (b) finely polished with liquid Perspex polish or Oakey's "Tripoli Composition" buffing soap. An electrically driven buffing wheel equipped with a loose stitched linen pad and a solid linen pad is ideal for this purpose (Fig. 5).

Mounting Fluid.—This is composed as follows: 30 per cent. glycerine, 10 per cent. sodium acetate, 0.5 per cent. formalin, water to 100 ml. It is boiled to drive off dissolved air before the formalin and sodium hydrosulphite are added. The sodium hydrosulphite in amount equivalent to 1 per cent. of the total solution is added last of all.

Solid Perspex (Methyl Methacrylate) Mounting.—The mounting of ophthalmic specimens in solid Perspex has been tried with success but the method is found to have limitations which restrict its application. The specimen is cleared so that it loses its natural appearance, and the contraction of the Perspex as it solidifies is apt to compress and distort the specimen. This method is, however, useful for mounting such specimens as portions of fragile bone, foreign bodies, and solid tumours.

*Materials Required.** — These comprise methyl methacrylate monomer ("Kallodoc" I.C.I.), benzoyl peroxide (catalyst), dibutyl phthalate (plasticizer), sodium hydroxide.

During manufacture the methyl methacrylate monomer is stabilized by the addition of hydro-quinone, and this must be removed before use with caustic soda.

Washing the Monomer.—Equal quantities of monomer and 5 per cent. caustic soda are poured into a separating funnel, well fixed, and allowed to settle. The discoloured washings which form a layer below the monomer are then run off. This is repeated three times, after which the washings should be colourless. The monomer is then washed with water until the washings are neutral to phenophthalein; it is then dehydrated with flaked calcium chloride for 24 hours. After filtering through filter paper it is ready for thickening; if not required immediately it may be stored in a refrigerator.

Thickening the Monomer.—A mixture of washed monomer 85 parts (by volume), dibutyl phthalate 15 parts (by volume), and benzoyl peroxide 0.1 per cent. (by weight), is placed in a flask (which should be only half filled) and partially polymerized on a boiling water bath for 15 to 30 minutes. The time depends upon the thickness of the syrup required. Three or four shakings are necessary during the heating. These should be carried out with great care as the reaction is

* Obtainable from Imperial Chemical Industries, Gloucester House, 149, Park Lane, London, W.1.

FIG. 5.—The joints of the box are rounded with a fine file and the whole container is then polished. The museum number on the inside is clearly visible.

FIG. 6.—Melanoma of the choroid. The specimen is mounted in solid Perspex.

FIG. 7.—Retrolental fibroplasia. The specimen has not been cleared and is mounted in solid Marco resin.

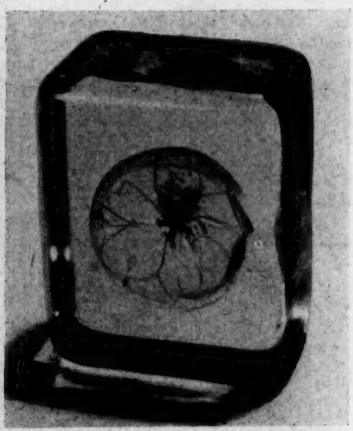

FIG. 8.—Diabetic retina injected with Indian ink; rete mirabile may be seen near the disk. The specimen is cleared and mounted whole in solid Marco resin.

exothermic and may cause the reaction to become violent; if this should happen the flask should be plunged into a sink of cold water kept ready for the purpose. The monomer is thickened to the maximum convenient viscosity (it should be remembered that the syrup will thicken further on cooling) and stored in the refrigerator.

Moulds.—Convenient moulds are made from glass slides of appropriate size bound together with cellophane or sealed with Semmentum.

Preparation of the Specimen.—The specimen is thoroughly dehydrated (any trace of residual moisture causes clouding of the Perspex) through graded alcohols, then placed in thin monomer (1 part of thickened monomer, 3 parts of chloroform) in a jar in a vacuum tank which is evacuated by a pump giving a vacuum of 24 in. Hg; bubbles will rise from the specimen. It should be left under vacuum for 24 hours, re-evacuating from time to time. The thin monomer is now replaced by semi-thick monomer (3 parts of thick monomer, 1 part of chloroform approximately) and treated by vacuum for a further 24 hours.

While the specimen is being prepared as above, a thin layer of thick monomer is poured into the mould and polymerized by ultra-violet light or heat, starting at 40°C. and rising to 50°C. to accelerate the final hardening. When this initial layer and the specimen are ready, the latter is transferred on to the layer of hard monomer in the mould and covered with thick monomer. The specimen is then positioned, care being taken that no bubbles are trapped underneath. The mould is then replaced in the vacuum tank, evacuated, and left under vacuum at room temperature for 24 hours: it is then polymerized under vacuum at 40°C. until hard.

Finishing.—When hard the block is cut with a fine saw to obtain a symmetrical mount of the required size. The surface is polished with the finest possible emery papers and finished with a fine abrasive and high speed mop (Fig. 6).

Solid Resin Mounting.—Despite the yellow colour of resin it has proved to be the best and most practical solid mounting we have tried. It is very easy to work with and quickly prepared, and specimens may be mounted cleared or uncleared as required.*

Components.—These comprise "Marco Resin S.B.26C", monomer C, diethyl phthalate (plasticizer), H.C.H. (catalyst), accelerator E.

Preparation of Plastic.—Take (A) "Marco" resin 100 g., (B) H.C.H. catalyst 2 g., and Monomer C 44 ml. Dissolve the catalyst in the monomer, warming if required to 37°C. Add plasticizer 9 ml., filter through Whatman paper No. 1. Add (B) to (A) and stir gently to ensure thorough mixing. For use add 1 ml. accelerator E to the above mixture, stir gently and allow to stand a few minutes for any bubbles to disperse before use.‡

Moulds.—Specimens can be embedded in almost any container which does not leak. Boxes can conveniently be made of glass cut to size and bound together with cellophane tape or sealed with Semmentum glue. Cardboard boxes lined with cellophane or straight sided tins may be used.

Casting of the Specimen.—

(*a*) Divide the resin mixture into two equal parts. Add the necessary amount of accelerator E to one half, and after thorough dispersion, pour into a mould of convenient depth, according to the size required in the final block. This will set in about one hour at normal room temperature (it is not advisable to use a curing temperature higher than 40°C.). During this stage it is important to cover the mould so that the tacky surface is kept dust free.

*Marco polyester resin may be obtained from Scott Bader & Co., Ltd., 109, Kingsway, London, W.C.2 and the technique described is based upon the instructions supplied by them.

†This mixture is stable for 1-2 days at room temperature and 4-5 days in the refrigerator.

‡This final accelerated resin is stable for only 1-2 hours (approx.) at room temperature and 12 hours (approx.) in the refrigerator.

(*b*) Carefully place the specimen on the tacky surface of the first layer. Avoid touching the surface more than necessary.

(*c*) Take the remainder of the resin mixture, add the required amount of accelerator E, mix, and pour it slowly over the specimen. Sufficient resin should be used to submerge the specimen to a depth of at least ¼ in. Care should be taken not to trap any bubbles underneath the specimen.

(*d*) Allow this final layer of the casting to solidify in the refrigerator overnight and leave for a further 24 hours before removing the block from the mould.

(*e*) Wash the sticky surface with acetone. Cut the block to the size required and then rub down the surface with suitable grades of emery paper. Leave for a few days to set completely hard and polish with a fine abrasive and high-speed mop.

Pre-casting Treatment of the Specimen.—

For opaque specimens: (*a*) fix in 10 per cent. Formol saline;

(*b*) when casting, dry the surface of the specimen with absorbent material, and allow to dry in the air until it is just short of darkening;

(*c*) block in resin (Fig. 7).

For cleared specimens: (*a*) dehydrate with graded alcohols;

(*b*) leave in chloroform 24 hours;

(*c*) Clear in monomer C;

(*d*) block in resin (Fig. 8).

My thanks are due to Dr. Peter Hansell for the photographs. I am particularly indebted to my chief technician, Mr. G. E. Knight, who has largely been responsible for investigating these methods, and to Mr. D. Bedford and Mr. G. Sharman for further technical assistance.

REFERENCES

HACKETT, C. J., and NORMAN, W. A. (1950). *Trans. R. Soc. trop. Med. Hyg.*, **43**, 357.

NOTES

Honours

THE Council of the Ophthalmological Society of the United Kingdom announces that the Edward Nettleship Prize for 1950 has been awarded to Professor A. J. Ballantyne, LL.D., M.D., F.R.F.P.S.G.

Fellowship

THE Faculty of Medicine, University of Toronto, announces the renewal of the Fellowship in Ocular Genetics of the Canadian National Institute for the Blind. The grant is $2,000 for research in this field. This Fellowship was held during 1949-1950 by Dr. L. A. Probert, of Moose Jaw, Saskatchewan, who has been carrying on studies of the hereditary aspects of glaucoma. Dr. G. A. Thompson, of Richmond Hill, Ontario, has been appointed to continue these studies in 1951 through funds provided by this Fellowship.